Faculty of Engineering of University of Porto

Thermal Characterization of Flaps in Plastic and Reconstructive Surgery

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Abstract

The mastectomy is one of the most used treatment in breast cancer, and the breast reconstruction is a surgery that the woman resorts to be restored to her femininity. Associate to this invasive surgical procedure, there are complications such as the partial or total loss of flap due to the inadequate perfusion caused by incorrect ligation between the main perforator and internal mammary arteries. Thus, is extremely important to study the vascularization of flaps used in plastic and reconstructive surgery and monitor the flap in post-operative phase so that perfusion problems can be early detected and can be corrected saving the flap. This study can be performed by thermography. Burns are other area of plastic and reconstructive surgery, in which infrared thermography (IRT) has been pointed out as efficient technique for burn depth evaluation constituting an auxiliary method for surgeon who decide the specific treatment to apply in burned patient.

The IRT imaging technique has been widely used in medical applications, since it is non-invasive, non-ionizing, simple, quick, and capable of monitoring large areas of skin surface temperature becoming very attractive for monitoring and characterization of flaps and burn depth assessment in plastic and reconstructive surgery.

In this research, the flap vascularization was thermally characterized in mastectomized patient undergone to breast reconstruction and in healthy women for an additional study about of the breast thermal signature. For this propose, it was used the static and dynamic thermography. This is expected to contribute as good indicator for the surgical procedure and posterior recovery, helping to reduce its time and associated costs. In burned areas, it was studied the burn depth of different burn degrees using IRT and comparing it with the clinical evaluation method.

The results showed that the thermography was efficient in the monitoring of the mammary reconstruction and in the post-operative follow-up, in the healing process verification. In the burns the thermography determined the depth of the burn that corresponded with the clinical evaluation made by the surgeon. With wider research and more documentation provided, medical IRT can become a widely used imaging modality and a natural part of daily medical imaging practice.

Key-words: Breast Reconstruction, Burns, Plastic and Reconstructive Surgery, Thermography

Resumo

A mastectomia é um dos tratamentos mais utilizados no cancro da mama e a reconstrução mamária é uma cirurgia que a mulher recorre para ser devolvida a sua feminilidade. Associado e este procedimento cirúrgico invasivo, existem complicações inerentes tais como a perda parcial ou total do retalho devida à inadequada perfusão causada pela incorreta ligação entre a principal artéria perfurante e as artérias da região da mama. Por isso, é extremamente importante estudar a vascularização dos retalhos utilizados em cirurgia plástica e reconstrutiva e realizar a sua monitorização no pós-operatório, para que sejam detetados atempadamente problemas de perfusão possibilitando a sua correção de forma a salvar o retalho. Os queimados é outra área da cirurgia plástica e reconstrutiva em que a termografia tem tido destaque como uma técnica eficiente para a avaliação da profundidade da queimadura constituindo um método auxiliar para o cirurgião na decisão do tratamento específico a aplicar ao doente.

A técnica de imagem térmica por infravermelho tem sido amplamente usada na área médica em várias aplicações por ser não invasiva, não ionizante, simples, rápida e capaz de monitorizar a uma área alargada de temperatura à superfície da pele, tornando-se assim muito atrativa para a monitorização e caracterização dos retalhos usados em cirurgia plástica e reconstrutiva.

Neste estudo a vascularização dos retalhos vai ser caracterizada termicamente em pacientes mastectomizadas e submetidas a reconstrução mamária e em mulheres saudáveis para um estudo adicional sobre a caracterização térmica da mama. Para tal, vai ser usada a técnica da termografia estática e dinâmica. Disto será esperado um contributo na forma de indicador objetivo do procedimento de cirurgia e posterior recuperação, ajudando a reduzir o tempo e custos associados. Na área de queimados será estudada a profundidade das queimaduras de diferentes graus através do uso da termografia comparando com o método de avaliação clínica.

Os resultados obtidos demonstraram que a termografia foi eficiente na monitorização da reconstrução mamária e no acompanhamento do pós-operatório, na verificação do processo de cicatrização. Nas queimaduras a termografia determinou a profundidade da queimadura que correspondeu com a avaliação clínica. Com mais investigação e documentação, a termografia médica ganha potencial de se tornar uma modalidade de imagem complementar amplamente utilizada em cirurgia plástica e reconstrutiva.

Palavras-chave: Cirurgia Plástica e Reconstrutiva, Queimados, Reconstrução Mamária, Termografia

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Contents

List of Figures

List of Tables

Abbreviations e Symbols

AFG	Autologous Fat Grafting
ASPS	American Society of Plastic Surgeons
BCT	Breast Conservative Treatment
BMI	Body Mass Index
BR	Breast Reconstruction
BT	Burned Temperature
CDU	Color Doppler Ultrasonography
CTA	Computed Tomography Angiography
CHSJ	Centro Hospitalar de São João
DIEA	Deep Inferior Epigastric Artery
DIEAP	Deep Inferior Epigastric Artery Perforator
DIEP	Deep Inferior Epigastric Perforator
DIRT	Dynamic Infrared Thermography
EIQ	External Inferior Quadrant
ESQ	External Superior Quadrant
FCI	Fasciocutaneous Infragluteal
FDA	Federal Drug Administration
FEUP	Faculty of Engineering of University of Porto
FOV	Field of View
GAP	Gluteal Artery Perforator
HP	Healing Potential
IBR	Immediate Breast Reconstruction
ICG	Indocyanine Green
IDEAL	Immediate-Delayed Autologous
IGA	Inferior Gluteal Artery
IGAP	Inferior Gluteal Artery Perforator
IIQ	Internal Inferior Quadrant
IRT	Infrared Thermography
ISQ	Interior Inferior Quadrant
ISO	International Standardization Organization
LA-ICGFA	Laser-assisted Indocyanine Green Fluorescence Angiography

LD	*Latissimus Dorsi Myocutaneous* flap
LDI	Laser Doppler Imaging
LDPI	Laser Doppler Perfusion Imaging
LEIQ	Left External Inferior Quadrant
LESQ	Left External Superior Quadrant
LIIQ	Left Internal Inferior Quadrant
LISQ	Left Interior Inferior Quadrant
MRA	Magnetic Resonance Angiography
n.a.	not available
NEDT	Noise Equivalent Differential Temperature
NEL	Northeast Left Breast Quadrant
NER	Northeast Right Breast Quadrant
NIR	Near Infrared Imaging
NL	Nipple Left
NR	Nipple Right
NWL	Northwest Left Breast Quadrant
NWR	Northwest Right Breast Quadrant
REIQ	Right External Inferior Quadrant
RESQ	Right External Superior Quadrant
RIIQ	Right Internal Inferior Quadrant
RISQ	Right Interior Inferior Quadrant
SEA	Superior Epigastric Artery
SEL	Southeast Left Breast Quadrant
SER	Southeast Right Breast Quadrant
SGA	Superficial Gluteal Artery
SGAP	Superficial Gluteal Artery Perforator
SIA	Spectrophotometric Intracutaneous Analysis
SIEA	Superficial Inferior Epigastric Artery
SIEV	Superficial Inferior Epigastric Vessels
SWL	Southwest Left Breast Quadrant
SWR	Southwest Right Breast Quadrant
TDAP	Thoracodorsal Artery Perforator
TG	Thermography
TRAM	Transverse Rectus Abdominis Myocutaneous
US	Ultrasonography
UT	Unburned Temperature
UV	Ultraviolet
E	Emitted energy
T	Temperature
σ	Stefan-Boltzmann constant

ε	Emissivity
ΔT	In breast reconstruction is the difference of temperature value between right breast and left breast; In burns is the difference of temperature value between burned and unburned area

Chapter 1

Introduction

1.1. Background

Breast cancer is the main oncologic incident disease in the feminine sex. In Portugal, this disease presents a incidence rate of 118,5 per 100000 women being a growing concern [1]. The provided treatment to one third of the patients diagnosed with breast cancer is a mastectomy [2]. Despite the conservative therapy of breast being an attractive process for patients, mastectomy is most recommended in case of large tumors, multifocal tumors, and in cases of recurrence after conservative treatment [3]. Furthermore, the mastectomy is selected by patient who are afraid of recidivism of the disease associated to other type of therapy. In general, the mastectomy corresponds to 40% of breast cancer therapy [4]. After mastectomy, the woman is confronted with psychological trauma associated to the loss of breast and consequently the loss of her femininity, self-esteem, and changes in sexuality and her social and familiar behavior [5]. These are the main reasons that lead the woman to explore breast reconstruction with the intention of returning her self-esteem with the replacement of the lost volume, breast symmetry and set reconstruction of the aureole-nipple. The goal of breast reconstruction is to re-create a new breast mound that looks and feels natural, durable and can mature and change with the patient over time. Essentially, the breast reconstruction can be performed in two ways: implant based reconstruction and autologous reconstruction. Although implant based reconstruction is more widely performed, autologous reconstruction is seen as the preferable choice for a large group of patients. The procedural statistics of American Society of Plastic Surgeons (ASPS) revealed that approximately 25% of reconstructions are performed using autologous tissue and 75% are performed using prosthetic devices [6]. The breast reconstruction should be individualized at its best, taking into consideration the oncological aspects of tumor, neo-/adjuvant treatment, genetic predisposition and its timing (immediate or delayed reconstruction), patient's conditions and wishes. With several different techniques available, it is important to find a method that fits the specific needs of every individual patient. Autologous breast reconstruction provides well-vascularized muscle and skin to define a breast with more natural aspect than implant based reconstruction and morbidity at the donor site is minimal [7]. In this type of reconstruction, the patient's anatomy, specifically the main flaps and theirs perforators used for breast reconstruction, should be very well studied for the correct selection of donor site and the main perforator artery which blood supplies the flap. So, it is important to study the anatomy of donor sites in order to facilitate the selection of flaps. In breast surgery construction, the inadequate perfusion is considered the main cause of flap loss, which constitutes one of the most common complications. This type of complication is associated to non-adequate detection of flap perforators responsible for blood supply and due to incorrect ligation between main flap perforator and internal mammary arteries. Therefore, knowledge about the vascularization of the flap is one of the main aspects to be considered in breast reconstruction. In intent on understanding these microcirculatory patterns and reducing morbidities, surgeons partnered with engineering to develop specific tools, which would allow a better understanding and appreciation of the anatomy and perfusion in different phases of reconstruction. Today many techniques are used in each phase of breast reconstruction such as Computed Tomography Angiography (CTA), Doppler Ultrasonography, Magnetic Resonance Angiogram (MRA), Dynamic Infrared Thermography (DIRT) and others. The use of infrared thermography (IRT) in medical field was adopted from the principle that increase in temperature causes a higher amount of thermal radiation emitted. Thus, an increase in peripheral vascularity, which can be a sign of many pathological changes such as inflammation or deeper hypervascularization, being this easily detected by an infrared camera. These processes can be observed in form of static single image or through the thermal recovery process in response to thermal challenge, called dynamic infrared thermography (DIRT) [8].

Many studies, mentioned in the literature review, report that the IRT technique may help surgeons obtain detailed information on the vascularization of the flap and its main perforators so that there is minimal complications constituting a complementary method used in breast reconstruction. The analysis of the rate and pattern of rewarming is an indicator of the underlying skin and subcutaneous tissue perfusion in pre-, intra-, and postoperative phase of breast reconstruction [9]. The use of DIRT in preoperative phase allows a qualitative assessment of perforators to the different flaps providing valuable information about flap vascularization for planning and designing tissue. The intraoperative use of DIRT provides important information on flap perfusion during free perforator flap surgery. In postoperative phase, the use of DIRT can reveal the perfusion of flap during the first operative week and in case of inadequate perfusion, can be detected and corrected avoiding the loss of the flap [10]. This may also be useful for identification of early necrosis at the edges of the attached flaps that reconstructed the breast [11].

The burns are another plastic and reconstructive surgery are, were IRT can be useful in early assessment of burns. The burns can be classified according to the depth of injury: I° superficial, IIa° superficial dermal, and IIb° deep dermal and III° full thickness. The determination of burn depth and verification if the burn healing process within 3 weeks or not is an important and crucial information for the surgeon, who has to decide the appropriate treatment: conservative or surgical. This information must be obtained early for a success recovery of patient. So, there is the need to monitor the burns and assess early for apply the specific treatment. Several modalities for burn depth assessment exist such as clinical evaluation, biopsy or Doppler but are either expensive or invasive or have a low accuracy. The IRT has been identified as a non-invasive, inexpensive technique with high accuracy in the evaluation of burn depth, constituting an excellent complementary method to assist the surgeon in the decision of the most suitable treatment for the patient.

1.2. Aim

This research aims to characterize the utility of thermography technique in plastic and reconstructive surgery. For this purpose, thermophysiologic changes are expected to be measured in affected areas to verify the procedure used. In this dissertation, it is expected to obtain the thermal characterization of healthy breast and identify the perforators vessels of flaps used in breast reconstruction. Furthermore, the post-surgical thermal modifications are analysed and compared with the complications associated to the breast reconstruction. In this work, the best method of external thermal challenge is assessed to use in dynamic thermography procedure. In burned patients, the determination of burn depth with IRT is employed, verifying the bilateral thermal symmetry and compare it with previous works.

1.3. Structure of the Report

In this section, it is briefly described the composition of the dissertation in which this research is structured.

Chapter 2, Literature Review where are described all relevant subjects for the performing this dissertation:

2.1, Fundamentals of breast, describes the anatomy, the main structures of the breast, the main quadrants in which the breast is divided, the all irrigation of mammary region, and the description of breast dermatomes.

2.2, Options of breast reconstruction, in this section is presented the two methods of breast reconstruction: implant and autologous reconstruction where are described the main flaps used in breast reconstruction, its vascularization, advantages and disadvantages of each method, definition of other two methods: reconstruction with acellular dermis and with fat graft, and finally the description of timing of the reconstruction with advantages and disadvantages.

2.3, Imaging technologies used in breast reconstruction, describes the different techniques used in breast reconstruction namely Computed Tomographic Angiography (CTA), Magnetic Resonance Angiography (MRA), Doppler Ultrasonography (Doppler US), Thermography (TG), are present the advantages and disadvantages of each method as well as the comparison between different modalities.

2.4, Thermography, describes the physical principles of thermography, the processes of thermoregulation in humans, the mechanisms that result in heat transfer caused by the human-environment interface standardization of the technique and dynamic thermography.

2.5, The use of DIRT in each phase of breast reconstruction: pre, intra e postoperative.

2.6, Burns, describes the anatomy of skin, the different types of burns according to the depth and different modalities of burn assessment and detailed description of burn assessment using static and dynamic thermography.

Chapter 3, Methodology, describes the methods, the equipment and software that will be used.

Chapter 4, Results and Discussion, in this chapter are presented the clinical cases of study, its analysis and discussion for each clinical case of study.

Chapter 5, Conclusion and Future Work, the main conclusion of results obtained and the proposals for future work to improve this project are presented.

In next figure are presented the relationship of different contents of this dissertation.

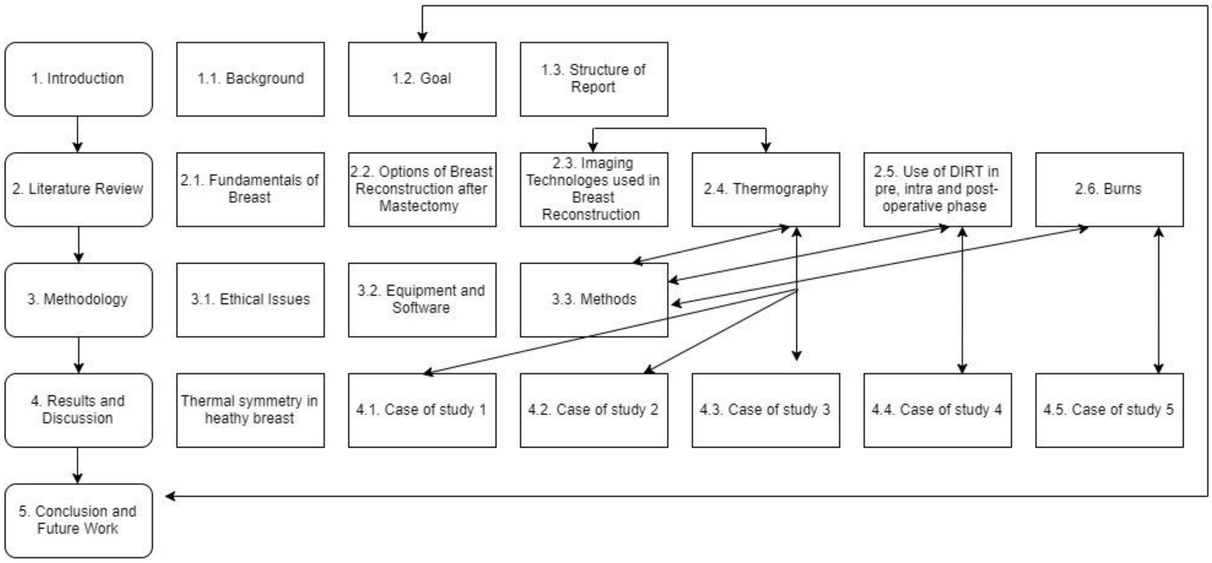


Figure 1.3.1: Relational schema of contents of dissertation.

Chapter 2

Literature Review

The literature review is composed by six subjects that are considered important for the execution of this work. The first theme is about the anatomy and physiology of healthy female breast. The second corresponds to the several techniques used in breast reconstruction including the type of used material: implant and autologous tissue. The various flaps are described with the advantages or disadvantages as well as the different times in which the reconstruction can be made. The third subject are the different methodologies used to discover the main arteries of the flap, only in breast reconstruction of free flap. In the fourth subject is described in detail about thermography: Thermal physics and physiology, heat transfer processes, standardization, limitations, and static and dynamic thermography. The fifth subchapter refers to the usefulness and the way of using dynamic thermography, namely to the methods of stimulation reported by different authors. The six subject corresponds to the burns: the anatomy of the skin, the division of burns, and the use of thermography in burn depth assessment.

2.1. Fundamentals of Breast

2.1.1. Breast Anatomy

The breasts are glandular structures located in anterior and posterior wall of thorax, each breast rests on the pectoralis major muscle, supported by ligaments of the sternum, the Cooper's suspensory ligaments, see figure 2.1.1. The breasts are derived from modified swear glands without capsule or special sheath, being a characteristic of the mammals destined to the segregation of milk for the new-born [12].

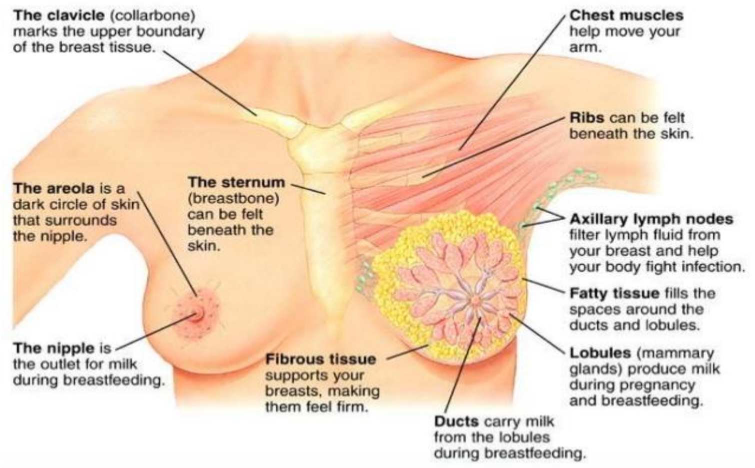


Figure 2.1.1: Localization of breast [13].

The breast size varies from woman to woman and inclusively, in the same woman depending on the age and the influence of diverse hormones [14]. Throughout its development the breast is undergoes in changes in its composition occurring a slow and progressive replacement of fibroglandular tissue by adipose tissue. Superficially, the breast has a small elevation in the central region, the nipple, which has a cylindrical or conical shape and is constituted by a set of ductal orifices, called lactiferous orifices [15]. The surrounding region of the lighter coloured nipple is the halo. Figure 2.1.2 shows the superficial anatomy of the breast.

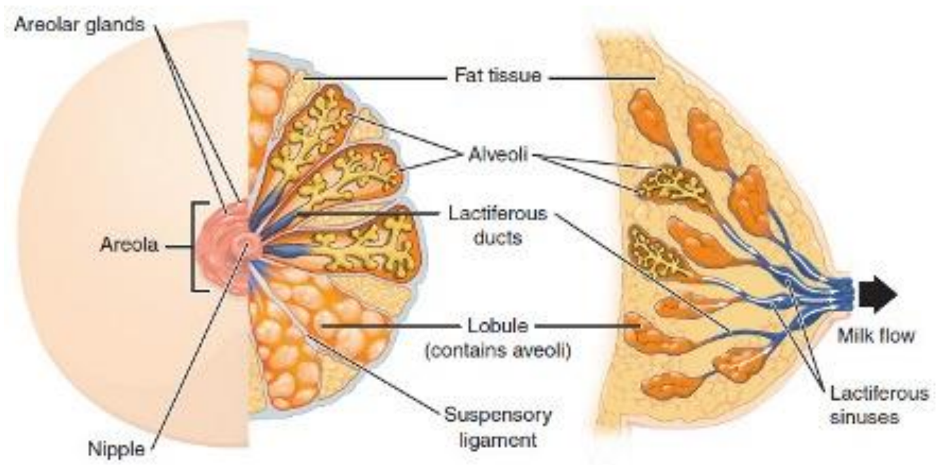
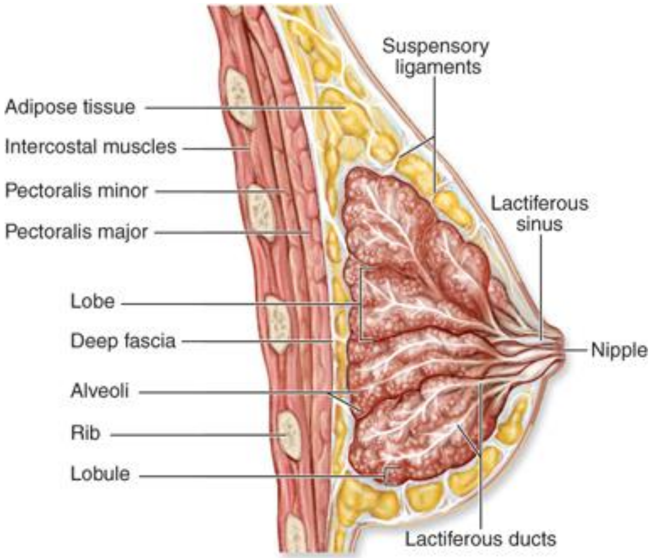


Figure 2.1.2: Superficial anatomy of the breast.

In terms of the anatomic constitution, the breast is formed by epithelial glandular tissue, adipose tissue and fibrous tissue that crosses and surrounds the glandular tissue [16]. The glandular tissue is tubule-alveolar and has 15 to 20 lobes that divides into lobes joined by connective tissue supporting blood vessels and ducts. The smaller lobes are constituted by the clusters of alveoli, which posteriorly separate to form terminal galactophores ducts [17]. Each of the ducts dilates in a small ampoule that works as a reservoir of milk shortly before ending in a tiny opening in the nipple area. The subcutaneous celluloadipous tissue covers the gland completely and is described in two parts: anterior and posterior. The anterior zone corresponds to the superficial area, located between the gland and the skin, where the adipose tissue is extended to the depth filling the spaces and furrows separating the lobes to the surface out of the areolar plane. The posterior is called the serosal pouch or retromammary space between the base of the gland and aponeurosis. The fibrous connective tissue extends from the retromammary serosal pouch to the dermis through the lobes and the lactiferous canals. It helps support the lobes and dominates as the suspensory ligament of the breast [18]. The figure 2.1.3 shows the detailed constitution of breast.



Source: Howard M. Reisner: Pathology: A Modern Case Study
www.accessmedicine.com

Figure 2.1.3: Sagittal cut of the breast.

2.1.2. Methods of Breast Localization

The quadrants are the most common division method for breast analysis. This method uses the nipple as a center resulting in four quadrants shown in figure 2.1.4, which are:

LQIE- Left External Inferior Quadrant	RQIE- Right External Inferior Quadrant
LQII- Left Internal Inferior Quadrant	RQII- Right Internal Inferior Quadrant
LQSE- Left External Superior Quadrant	RQSE- Right External Superior Quadrant
LQSI- Left Internal Superior Quadrant	RQSI- Right Internal Superior Quadrant

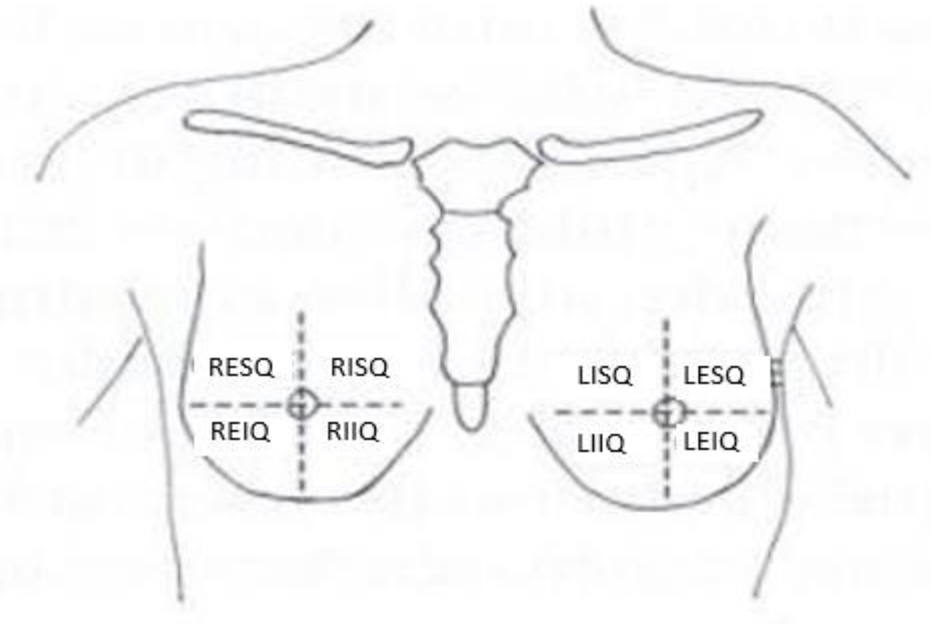


Figure 2.1.4: Identification of breast quadrants [14].

2.1.3. Breast Vascular Irrigation

The breast is irrigated by a vast arterial, venous and lymphatic network.

- **Arterial Vascularization**- Corresponds to the vascular flux that crosses the internal part of gland by penetrating ramifications of the internal mammary artery, which passes through the six intercostal spaces. The main arterial branch reaches the breast through the second intercostal space. The irrigation comes from the upper thoracic arteries, the lateral thoraco-acromial, internal thoracic and posterior intercostal arteries. The external and inferior parts are fed by the ramifications of the external mammary artery, as well as the lower scapular, the thoraco-acromial and the upper thoracic arteries. The lateral descends by the lateral edge of the small pectoral muscle giving origin to lateral mammary branches that arrive at the breast by the lateral edge. The internal thoracic artery, the subclavian branch during its course produces perforating branches originating medial mammary arteries that will reach the gland [12], [19]. The figure 2.1.5 shows the main arteries responsible for arterial vascularization.

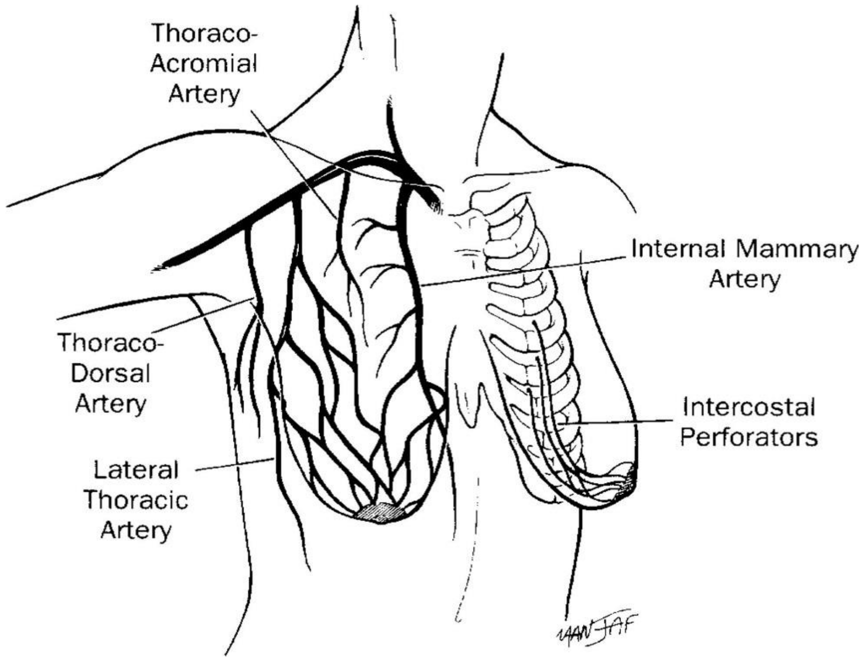


Figure 2.1.5: Arterial Vascularization of the breast.

- **Venous Vascularization**: This type of vascularization presents a path near the path of the arteries and directs to the axillary, internal thoracic and superficial of abdomen veins [18]. In addition to these, there are deep veins that cross the large pectoralis muscle and drain into the intercostal veins. The venous network terminates its course in the external mammary veins, the internal and intercostal mammary vein. The main veins are presented in figure 2.1.6.

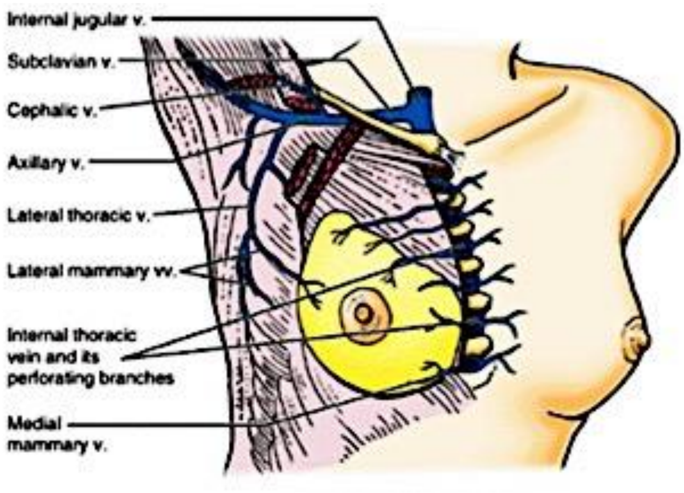


Figure 2.1.6: Venous drainage of the breast.

- **Lymphatic irrigation:** has three ways: collecting network of axillary ganglia, relative network of internal mammary glands and collecting network from supraclavicular ganglia [18]. Figure 2.1.7 shows the breast lymphatic drainage.

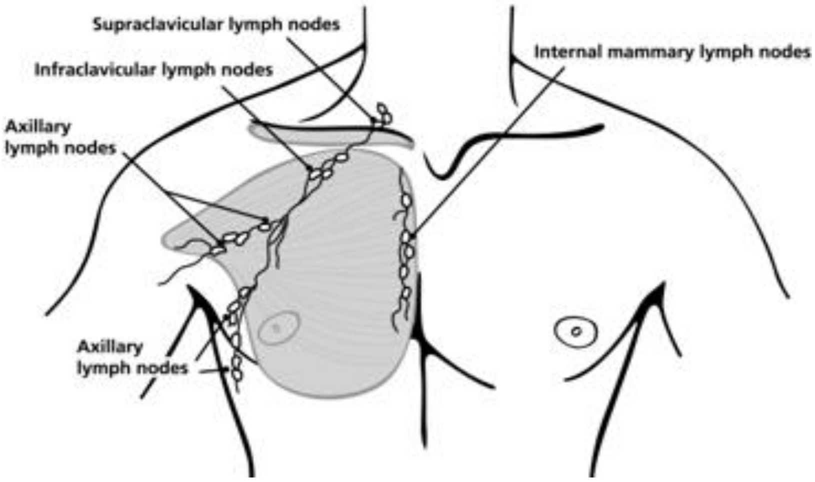


Figure 2.1.7: Lymphatic drainage of the breast.

2.1.4. Breast Dermatomes

A dermatome corresponds to a skin area that is innervated by nervous fibres from the spine. Each dermatome refers to a spinal nerve that innervates it. When stimulating specific regions of skin surface, called dermatomes points occur depth nervous reactions because the correspondent regions of spinal cord are stimulated directly and consequently the structures of human body innervated by the set of nerves of this area. In breast region the nervous fibres correspond to the totally dermatome T4 and partially dermatomes T3 and T5 [20]. The breasts dermatomes are presented in figure 2.1.8.

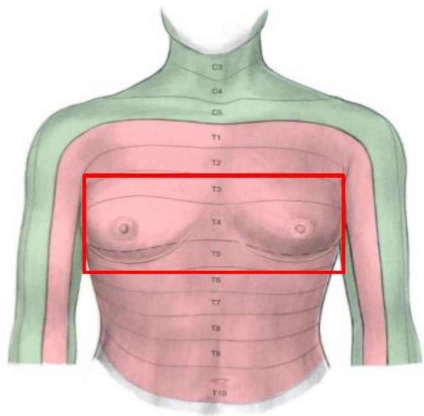


Figure 2.1.8: Breasts Dermatomes [21].

2.2. Options of Breast Reconstruction after Mastectomy

In breast reconstruction a choice of non-autologous or autologous material and the timing of reconstruction has to be taken into consideration [22]:

- **Implant vs. autologous reconstruction**
- **Immediate vs. delayed reconstruction**

There are different options of breast reconstruction and it can be classified into three categories:

- **Implant and Expander-based breast reconstruction -** The use of prosthetic material (non-autologous material);
- **Flap-based breast reconstruction -** The use of material from the patient body (vascularized autologous material) or the combination of these options (flap and implant);
- **Fat Graft-based breast reconstruction** (non-vascularized autologous lipoaspirate fat).

Table 2.2.1 presents the general comparison between implant- based and autologous tissue-based breast reconstruction. This table is based on table 1 of Schmauss, Machens, and Harder [23] reference literature source.

Table 2.2.1: Comparison between implant- based and autologous tissue-based breast reconstruction its advantages and disadvantages.

Option Breast Reconstruction	Implant based	Autologous tissue based
Advantages	Surgery time is smaller; Requires less infrastructural effort; Low surgical complexity; No need of donor site.	Reconstruction with autologous tissue is preferable to implant based in adjuvant radiotherapy [24]–[26]; Lower complications rate in long term; Lower reoperation rate in long term; Higher patient satisfaction.
Disadvantages	In case of insufficient soft tissue coverage, there is the need of acellular dermis matrix (ADM) leading to inferior standard results. Higher complications rate in long term due to capsular contracture after radiotherapy; Higher reoperation rate involving capsular removement and implant changes [24], [27].	Surgery time is longer; Requires more infrastructural effort; High surgical complexity; Need donor site and depend on the flap selected.

2.2.1. Implant and Expander-based Breast Reconstruction

Reconstructive techniques use some types of prosthetic material such as silicone or saline fill with different shape and texture [2], [3]. In case of the use of these materials can be adopted two different techniques: Implant-Based Breast Reconstruction and Expander-Based Breast Reconstruction. The first corresponds to the immediate implant placement and this procedure requires that skin flaps post-mastectomy be sufficient to cover the implant. The other is used when the skin flaps are not enough to cover the implant and involves tissue expansion followed by permanent implant placement. In the table 2.2.2 are presented the main features of this breast reconstruction option:

Table 2.2.2: Table of prosthetic material characterization.

Procedure	Without Tissue Expander	With Tissue Expander
Target Patient	Patients who do not qualify for autologous reconstruction, or do not want additional scars; with small breast and prefer quicker postoperative recovery period.	
Contraindications	Patients exposed or future undergone to radiotherapy [2], [28]-[30]; Obesity; Thin skin; Rheumatologic diseases [30].	
Advantages	Simple operation; Donor site morbidity avoidance [31]-[34]; Less operative time and recovery period than autologous reconstruction.	
Disadvantages	Greatly increased risk of skin necrosis secondary to tension; Poor aesthetically results [31]; Risk of infection, disruption, extrusion or capsular contracture [35]; Implants lack natural ptosis and feel unnatural [31].	Overall time required; Greatly increased risk of skin necrosis secondary to tension; Poor aesthetically results [31]; Risk of infection, disruption, extrusion or capsular contracture [35]; Implants lack natural ptosis and feel unnatural [31].
Complications	41 % of patients exposed to radiotherapy present pain, capsular contracture, exposition and elimination of implant compared with 12% of patients that present these complications but not realized radiotherapy [36].	Short term complications require removal of expander or implant including exposure of the device to infection, malposition or deflation [31]; Hematoma or seroma; Long term complications include capsular contracture, visible wrinkling of the implant; Complications associated to a radiation corresponds to 50% [30], [37], [38].

2.2.2. Flap-based Breast Reconstruction

The selection of appropriate flap tissue must take into account the amount of required tissue, available tissue in donor site, patient’s lifestyle and associated pathology [4].

A perforator flap is a piece of skin and subcutaneous tissue that is transferred from one part of body to another in the same patient. The blood vessels that supply the flap are called perforators. Each perforator consists of one artery and vein [10].

The breast reconstruction with autologous tissue can be classified into two categories the pedicle flap and free flap. The pedicle flap consists of the tissue which is left partly attached to the "donor site" and transferred to a new part of body in close vicinity, keeping the pedicle intact ensuring continuous blood supply. The free flap has to be cut to enable the transfer of the flap to a "defect site" at a longer distance. In this case the tissue and its blood supply is fully detached from donor site and transposed to the "defect site". After the flap has been transferred the blood supply to the flap, is re-established by anastomosis of arteries and veins [10]. This type of procedure is considered a good method after radiotherapy [24]-[26]. In case of radiotherapy following autologous reconstruction, there are disadvantages such as poor aesthetical results and skin fibrosis [22].

The different autologous materials commonly used in breast reconstruction are:

- LD- *Latissimus Dorsi Myocutaneous flap;*
- TRAM- Transverse Rectus Abdominis Myocutaneous flap;
- DIEAP- Deep Inferior Epigastric Artery Perforator flap;
- SIEA- Superficial Inferior Epigastric Artery Perforator flap;
- GAP-Gluteal Artery Perforator flap;
- IGAP- Inferior Gluteal Artery Perforator flap;
- SGAP- Superior Gluteal Artery Perforator flap;
- FCI – Fasciocutaneous Infragluteal flap;
- TDAP- Thoracodorsal Artery Perforator flap.

Lower abdomen flaps

The flaps from the lower abdomen are the first choice, being considered as the gold standard in breast reconstruction, because it offers tissue quality, texture and enough volume to create satisfying outcomes [39]–[41]. Furthermore, this procedure is referred as an attempt to reduce morbidity at the donor site [39]-[42] and there is an algorithm for selection of flaps from the lower abdomen for breast reconstruction proposed by Arnez, Khan, and Pogorelec [42]. The flaps used from this donor site are the free transverse rectus abdominis myocutaneous (TRAM), the deep inferior epigastric perforator (DIEP) and the superficial inferior epigastric artery (SIEA). There were studies that reported the successful use of this type of flaps in breast reconstruction [43]–[45].

TRAM-Transverse Rectus Abdominis Myocutaneous flap

The TRAM flap is composed of a lower abdominal skin, subcutaneous fat tissue and all or part of rectus abdominis muscle, see figure 2.2.1. The TRAM flap is supplied by the deep inferior (free flap) and superior epigastric arteries (pedicled flap) (figure 2.2.2). In addition, the blood supply is made by venae originating on the external iliac vessels just above the inguinal ligament. The innervation is ensured by intercostal nerves.

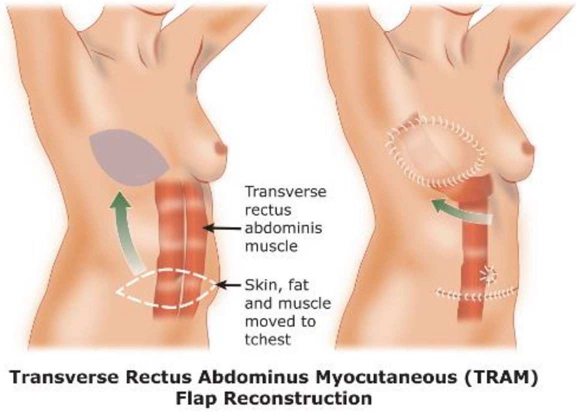


Figure 2.2.1: TRAM flap.

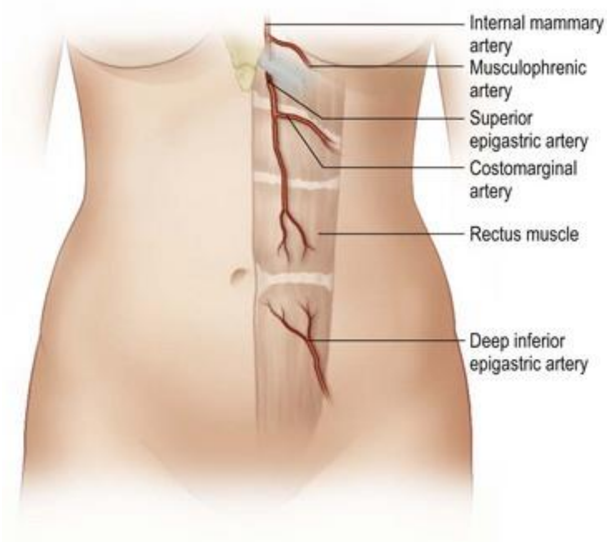


Figure 2.2.2: Vascular anatomy of abdomen.

There are different types of TRAM flaps and the table 2.2.3 resumes their mains characteristics:

- **Pedicle TRAM flap** – In this technique, the total rectus abdominus muscle is tunneled underneath the skin of the upper abdomen and transferred up the mastectomy site [46]. This procedure uses the deep superior epigastric artery (DSEA) in the muscle tissue to supply blood in the breast reconstructed. In figure 2.2.3 is presented this type of flap.

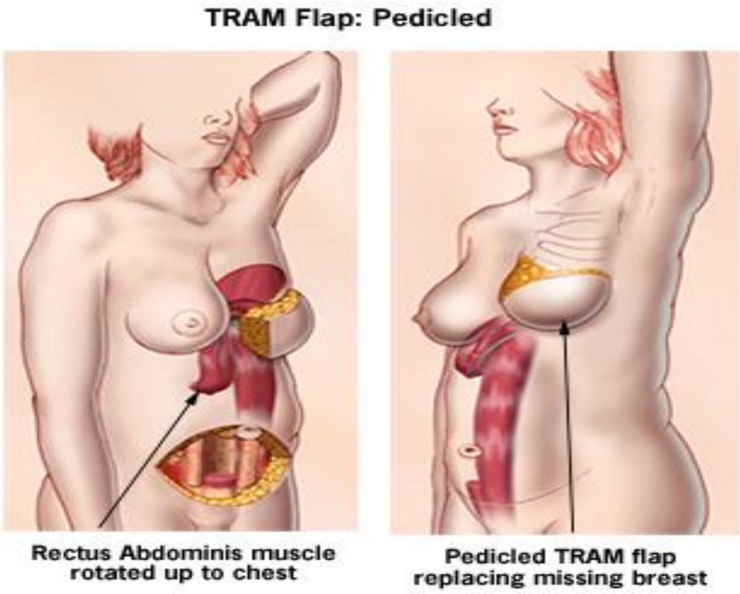


Figure 2.2.3: Pedicled TRAM flap.

The pedicle TRAM flap is the most common pedicled skin-muscle flaps used in reconstructive surgery [11]. There are two methods for breast reconstruction using pedicle TRAM flap and the choice depends on surgeon's experience and patient's anatomy.

- **IPSI lateral flap** - this procedure involves less tension but more flap pedicle rotation [47] where skin flap of rectus abdominis muscle is harvested with muscle that is located at the same side as the defect breast. This operation is applied in cases which scars preclude use of the contralateral pedicle. Clugston *et al*. [48] presents many advantages associated with the use of this method such as simplicity and versatility of flap shaping, improved maintenance of the inframammary fold, less pedicle tension during inset, less bulk of muscle from split muscle harvest, flap reliability and a lower incidence of partial flap necrosis compared with the contralateral pedicle TRAM and others.
- **CONTRA lateral flap** - this method involves more tension but less flap pedicle rotation [47]. In this type the flap is extracted within the muscle diagonally and placed on the breast, where the deep superior epigastric pedicle is connected with internal thoracic artery [49]. The contralateral pedicle produces superior aesthetic results because it is transferred to the "defect" site through a tunnel along the contrary side of sternum. The split of muscle helps close the abdomen. On the other hand, this procedure may lead to disruption of the inframammary fold and the medial bulge caused by the transferred rectus muscle [7].

The importance of tension and rotation of vascular pedicle referring to IPSI flaps provides more favorable conditions to avoid future complications [50] such as development of necrosis. However, the results indicated by Jankau, Moderhak, and Kołacz [47], show that the mean intraoperative surface temperature and median of IPSI flaps are higher than CONTRA flaps and according to Francis *et al*. [51] its suggests better blood supply to the flap.

- **Free TRAM flap** – In this procedure, the deep inferior epigastric artery (DIEA) and associated veins are completely lacerated, transferred of the abdominal tissue to the breast defect and anastomosed microsurgically to the recipient vessels, internal mammary artery (IMA) or thoracodorsal artery (figure 2.2.4). Study performed by Fujino, Harashina, and Enomoto and trial by Holmström reported excellent results using the free TRAM flap [52], [53]. For Elliott et al. [54] the free TRAM flap is better than the pedicled TRAM flap technique for immediate breast reconstruction.

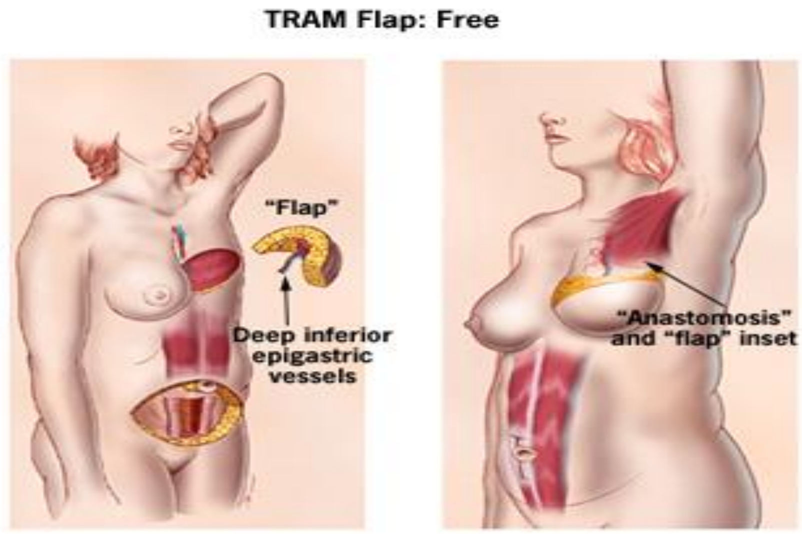


Figure 2.2.4: Free TRAM flap.

- **Muscle sparig (ms)-TRAM flap** – In this procedure, only a small cut of muscle around the vascular pedicle.

Table 2.2.3: Table of TRAM flaps characterization

Flap Name	Pedicle TRAM	Free TRAM
Target Patient	Patient who have a normal, big and ptotic contralateral breast and sufficient lower abdominal tissue [31].	
Contraindications	Prior abdominal surgery, cholecystectomy, coronary artery bypass and others surgical interventions [55]; smoking habits [56]; obesity [57]; age > 65; severe comorbidities such as vascular diseases, diabetes mellitus DPOC, etc. [3], [31].	Smoking habits [56]; obesity [57]; age > 65; severe comorbidities such as vascular diseases, diabetes mellitus DPOC, etc. [3], [31].
Advantages	Do not need the use of prosthesis; Natural aspect [3]; Single time surgical; Improving the abdominal contour; Changes the size of breast according to weight changes [31]; Good healing process and scar wispy visible [58].	Do not need the use of prosthesis [3]; Natural aspect; Single time surgical; Improving the abdominal contour; Changes the size of breast according to weight changes [31]; Good healing process and scar wispy visible [58]; This procedure can be used when the superior epigastric artery has been divided (patient who has had a previous open cholecystectomy); Provides more robust blood supply [31]; Greater preservation of rectus abdominis muscle than pedicled flap [59]; Less fat necrosis, preservation of the inframammary fold, freedom of flap orientation and reduced donor-site morbidity [7].
Disadvantages	Potentially longer operating time and the need microsurgical expertise; high amount of blood loss [55]; Long time of hospitalization and postoperative recovery [60]; Significant donor site morbidity [55]; Whole rectus abdominis muscle is incorporated into the flap.	More demanding than pedicle TRAM; Potentially longer operating time and the need microsurgical expertise [55]; High amount of blood loss; Long time of hospitalization and postoperative recovery; In secondary reconstructions (especially in radiated cases), dissection of axillary vessels is very difficult; The thoracodorsal artery frequently is small and sometimes found to have insufficient flow, necessitating anastomosis to the circumflex scapular artery more proximal in the subscapular system. The arterial anastomosis can avulse with shoulder motion. Anastomosis in the axilla is technically difficult for the assistant, because he or she is operating across the chest [7].

Complications	In the short term includes infection (12%), hematoma or seroma of the breast or abdomen (4 %), umbilical necrosis, partial loss (16%) and total loss (1%) [57]. In the long term include abdominal wall laxity or hernia (8%); Donor-site complications occurred in 35,5% of patients, flap necrosis in 9,8%, fat necrosis in 17,9% and abdominal hernia in 1,5%. Smokers present a higher rate of pedicle TRAM flap infection [61].	In the short term include infection (18%), hematoma or seroma of the breast or abdomen (4.5-9%), umbilical necrosis, partial loss (15%) and total loss (1.5%); In the long term include abdominal wall laxity or hernia (12%) [57]. Flap complication occurred in 23,7% of flaps and donor-site complication in 14,8% of patients [62].

Four zones of the blood supply can be distinguished in TRAM flap. This division is based on the different perfusion according to different zones. The zone I provides the most reliable zone for reconstruction. In zone II and III the blood perfusion depends on the anatomy of each patient. Zone IV is considered to be a poor blood perfusion zone and it is usually discarded for reconstruction surgery because it can lead to necrosis [11], [46]. The division into zones is not precise and identification of the zones depends on the surgeon’s experience [11]. Abdominal skin flap was described by Hartrampf [46] as shown in the figure 2.2.5.

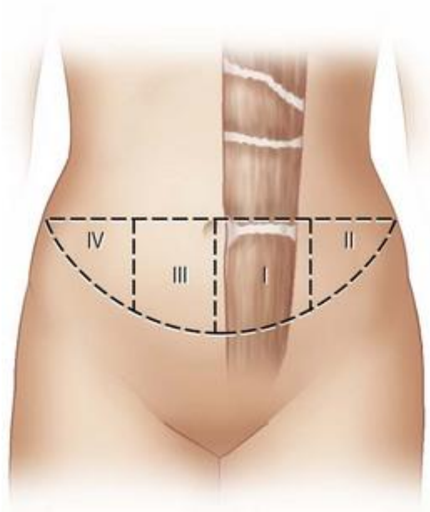


Figure 2.2.5: Four zones of the blood supply in the abdominal skin flap [63].

DIEP- Deep Inferior Epigastric Perforator flap

Although multiple free flap procedures have been performed, similar to free TRAM flap, the DIEP flap is the most feasible free flap and constitutes the gold standard in autologous breast reconstruction [22]. There are many studies [64]-[67], which report the excellent results using the

DIEP flap in breast reconstruction. This technique is similar to TRAM flap because utilizes the same skin island but DIEP flap does not require the harvested of the abdominal rectus muscle. The DIEP flap include all the advantages of the free transverse rectus abdominal myocutaneous (TRAM) flap, also considered a good choice in breast reconstruction, but DIEP flap no presents the donor site complications including abdominal hernias and weakness of the abdomen [68]. In order to minimize donor-site morbidity, pain, and recovery time, the muscle fibers are separated longitudinally without dissecting, which leads to preservation of intercostal nerves. The blood supply of this flap is based on 3-7 large perforators from the Deep Inferior Epigastric Artery (DIEA) that are concentrated in the periumbilical region (figure 2.2.6). There are two main intramuscular branches, the lateral branch and medial branch represented in figure 2.2.7. The lateral branch is reported by Itoh and Arai [69] to be in 88,2% the most dominant branch of DIEA. This branch provides a lateral row of perforators in the lateral third of the muscle, and the anastomoses occurs with lower four intercostal arteries. The second, provides a medial row of perforators in the medial third of the muscle, also gives off an umbilical branch before terminating in choke vessel anastomoses with the Superior Epigastric Artery (SEA) above the umbilicus. Other study performed by Blondeel *et al*. [70] revealed that the diameter and flow velocities of a dominant lateral branch were statistically higher than those of a dominant medial branch. Furthermore, majority of lateral row perforators (71,4%) have a rectilinear course comparing with medial row perforators (18,2%) [71]. On the other hand, the studies of Figus, Ramakrishnan, and Rubino and Masia *et al*. [72], [73] reported that the DIEP flap is mainly based on medial perforators, the chosen perforator had its origin in medial branch of DIEA in 61% [73]. If is necessary to include zone IV of abdomen, it is suggested that the selection of perforator is performed from the medial row. However, Weerd, Miland, and Mercer [74] that studied the perfusion dynamics of free DIEP flap revealed that the perforators from medial and lateral row are interconnected by true anastomosis and this finding suggests that perforators are within the same angiosome is in accordance to the concept of Taylor and Palmer [75]. The DIEP flap procedure, see figure 2.2.8, needs significant microsurgical expertise in perforator pedicle dissection to avoid damaging of the perforator vessels that can lead to compromised flap circulation [76] but despite these requirements the DIEP flap gets satisfactory results. The choice between the TRAM and the DIEP flap should be based in the vessel diameter, the caliber of pedicle, the location of perforating vessels, weight of patient, the breast volume, quality and amount of abdominal fat tissue [77]. Table 2.2.4 presents the main characteristics of the DIEP flap.

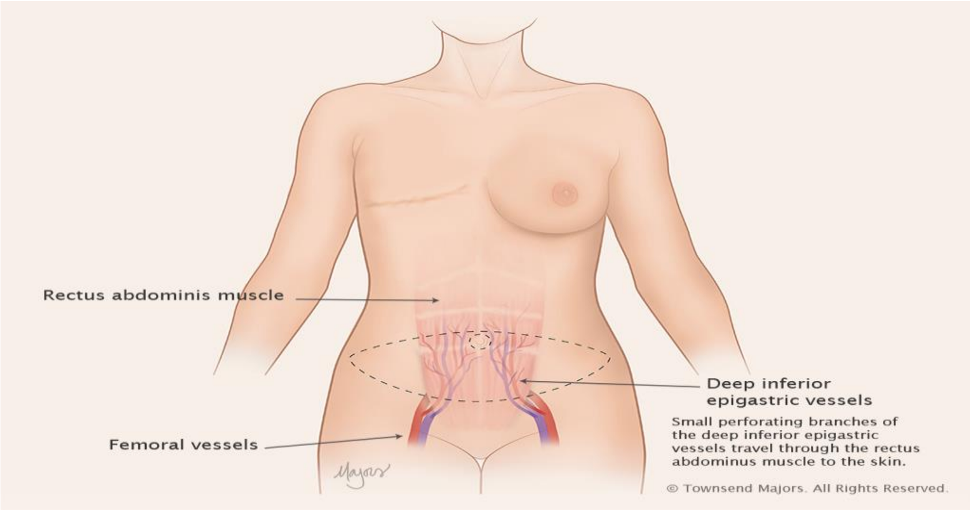


Figure 2.2.6: Vascular Anatomy of DIEP flap [78].

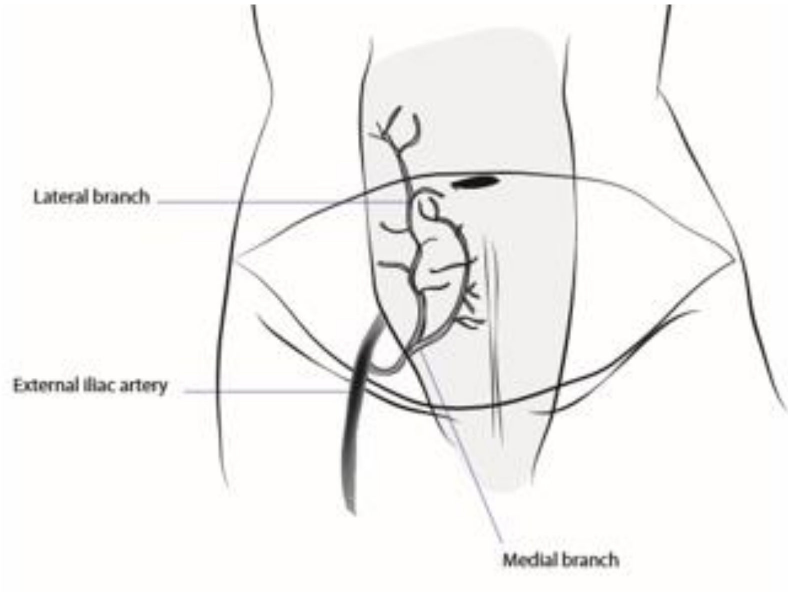


Figure 2.2.7: Intramuscular branches [7].

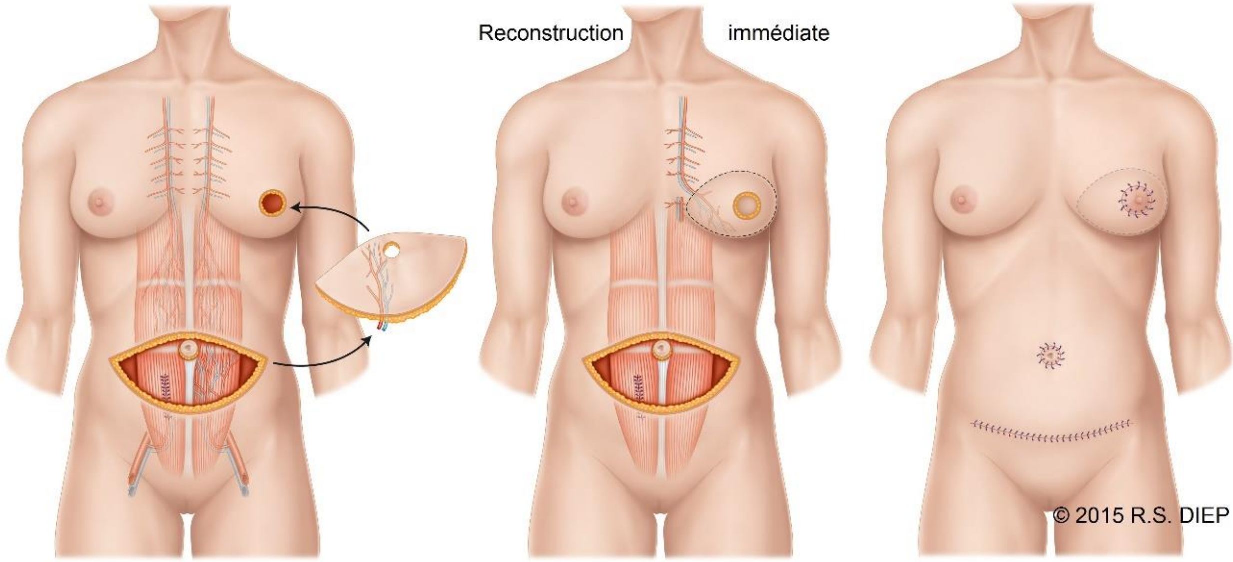


Figure 2.2.8: Breast reconstruction using DIEP flap [79].

Table 2.2.4: The main characteristics of the DIEP flap.

Flap name	DIEP
Target Patient	Reconstruction in patient with small breast or for those breasts that do not require more than 70 % of the abdominal flap to achieve adequate volume and shape [80].
Contraindications	History of previous abdominoplasty, liposuction or active smoking [7]; Large transverse or oblique abdominal incisions; Today, the real absolute contraindication are non-compliant patients or a poor general condition [41], [81].
Advantages	Total preservation of abdominal rectus muscle; Less abdominal wall morbidity; Less incidence of abdominal wall laxity or hernia or pain than others procedures that remove abdominal wall fascia with the rectus muscle; Short hospitalization and fast recovery resulting low costs [82]; Complications occur infrequently.
Disadvantages	Significant microsurgical expertise; Longer operative time; Less robust blood supply leading to an increased risk for fat necrosis [80].
Complications	2,5% of the partial flap loss; less than 1% of total flap loss [65]; Necrosis of the fat tissue and seroma formation; 1% of abdominal herniation [41], [65], [83].

Garvey *et al* [82] compared results of 190 women who had undergone unilateral breast reconstruction with 96 DIEP flaps and 94 pedicled TRAM flaps. In this study noted that the incidence of fat necrosis in the pedicled TRAM flap was 59% whereas this complication was 18% for reconstruction using DIEP flap. The incidence of the abdominal wall hernia was higher in pedicled TRAM group (16%) than DIEP flap (1%) and the rate of abdominal wall bulge was similar in both groups.

SIEA- Superficial Inferior Epigastric Artery flap

The SIEA flap is based on superficial inferior epigastric artery (SIEA) and superficial inferior epigastric vessels (SIEV) which arise from the common femoral artery and saphenous bulb. The studies of Boyd *et al*. [84] and Taylor *et al*. [85] report that the SIEA was absent in 35% of all cases and, on the other hand, Reardon *et al*. [86] demonstrated a patent SIEA in 91% of their reconstructions. The SIEA was located between 1 cm - 2.5 cm of the midpoint of the inguinal ligament and the pedicle length varies between 3 - 7 cm and the vessel caliber between 1.2-2.5 mm [86]. This type of flap keeps intact the rectus abdominis fascia and muscle [87]. Thus, the SIEA flap includes minimal donor site morbidity and eliminating the all-risk for postoperative motor weakness and herniation [85], [88]. So, the advantages are the same of DIEP flap. According to Munhoz *et al*. [89] no exists the immediate complications and after median 3.5 years no evidence of fat necrosis neither bulges or hernias were observed. Generally satisfactory outcomes are achieved. Chevray [66] demonstrated that in 14 SIEA reconstructions, one flap loss and two situations of partial flap necrosis. According to Granzow *et al*. [90], who realized 210 breast reconstruction using SIEA in 174 patients, demonstrated no flap loss, no hernias or unsightly abdominal bulges occurred. The fat necrosis occurred in 13% and donor site seromas occurred in 4%. In the same study, the arterial diameter of pedicled was 1.5 to 2.5 mm and the vein was 2 to 4 mm. In table 2.2.5 are presented the main characteristics of the SIEA flap and in figure 2.2.9 is shown the SIEA flap reconstruction.

Table 2.2.5: The main characteristics of the SIEA flap

Flap Name	SIEA
Advantages	Minimal donor site morbidity because the vessels are dissected at the level of Fascia Scarpa with no incision made at the Fascia Rectus [7]; The IM vessels (recipient site) are spared for possible future cardiac surgery, thoracic deformities are avoided; The limited dissection decreases operative time [89].
Disadvantages	Vessels are often not in appropriate caliber to sufficiently support the perfusion of the tissue volume needed [91]; High level of expertise in dissection of the vascular pedicle because of its variability existence, location and caliber [31]; The inconsistence vascular pedicle anatomy and the smaller diameter of the arterial pedicle.
Complications	2 % of the flap loss and higher rate of emergency reoperation for the SIEA flap compared with TRAM and DIEP [66].

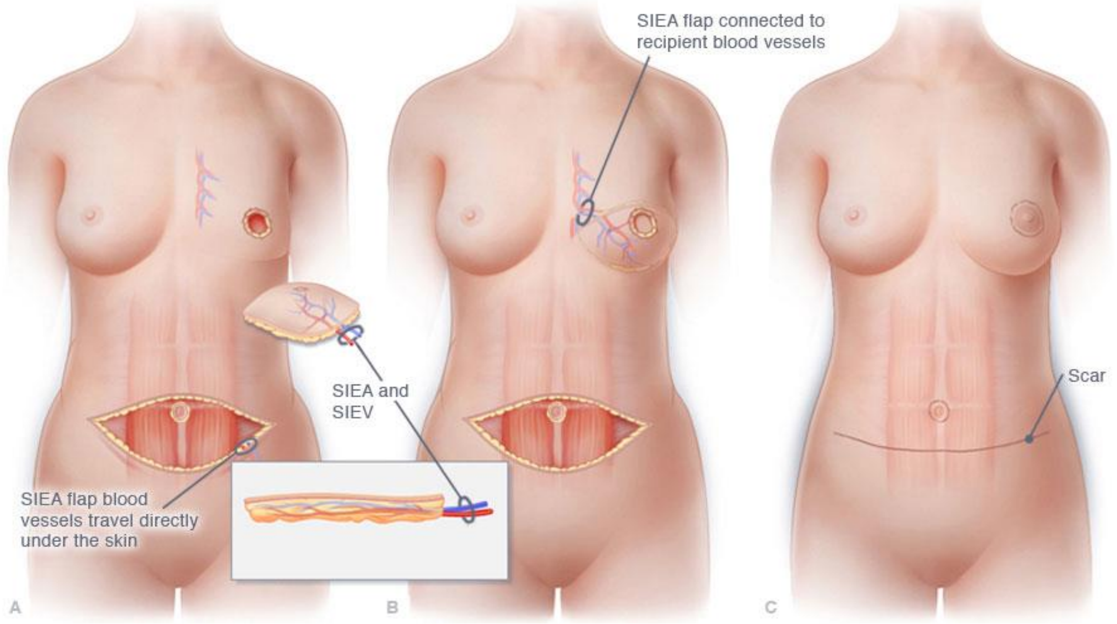


Figure 2.2.9: Breast reconstruction using SIEA flap [79].

LD- Latissimus Dorsi Myocutaneus flap

The LD flap consists of the skin and subcutaneous fat including the dorsal muscle. The blood supply of this flap is based on the thoracordorsal artery and vein (figure 2.2.10). This procedure, exemplified in figure 2.2.11, is often used in cases of lower abdominal flaps failure and can be transferred with its pedicle or as a free flap transfer. In case of first option, the flap is tunneled subcutaneously via axillar region and transferred up the mastectomy site. The majority of patients do not have enough tissue in dorsal region for breast reconstruction and so it is necessary to use the implant under the muscle [92]. The combination of implant and LD flap limits capsular contracture and visible rippling of prosthesis, contributing to a natural aspect and texture of breast. Furthermore, tissue expansion is not needed and secondary revision procedures are easier than by only implant option [7]. To minimize donor site morbidity and seroma formation, there are some variations of muscle amounts harvested (muscle sparing (ms)-LD) [93]. This option is ideal for breast reconstructions that need only skin and subcutaneous tissues. The ms-LD flap can be harvested to include only descending branch of the thoracodorsal artery which increases the reach of the skin paddle [7]. The other alternative autologous breast reconstruction is the thoracodorsal artery perforator (TDAP) flap which is similar to LD flap but does not include muscle. As described above the lower abdominal flap for breast reconstruction the gold standard however in many medical centers the LD flap is the first choice technique [55]. In table 2.2.6 are presented the characteristics of LD flap.

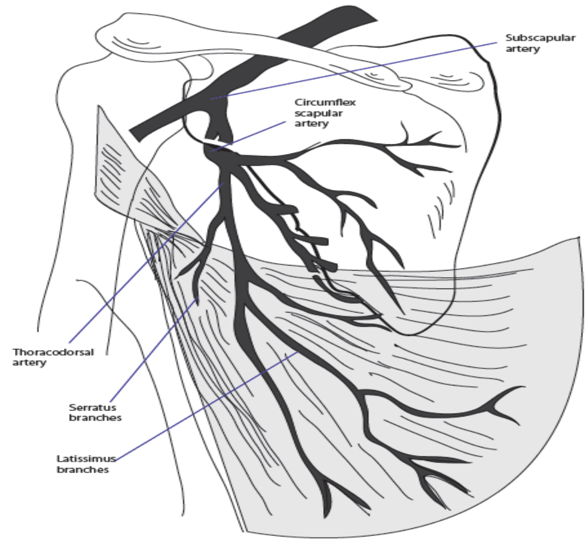


Figure 24. Vascular pedicle of latissimus dorsi musculocutaneous flap. (*Modified from Schusterman.*[177])

Figure 2.2.10: Vascular pedicle of LD flap [7].

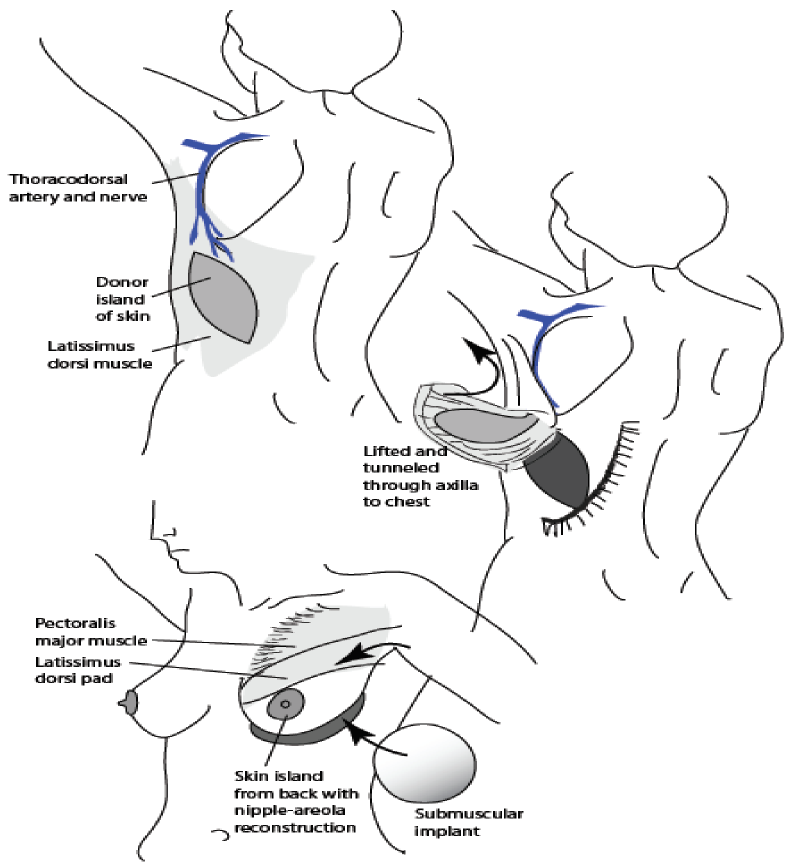


Figure 23. Technique of breast reconstruction with latissimus dorsi musculocutaneous flap over an implant.

Figure 2.2.11: Breast reconstruction using LD flap [7].

Table 2.2.6: Table of LD flap characterization.

Flap Name	LD
Patient Target	Patients with abdominal obesity or extreme thinness; Patients who do not want scars in abdominal regions; Patients with lower abdominal flaps failure [7].
Contraindications	Patients who have the thoracodorsal artery lacquered; Denervated and atrophic muscle; Severe comorbidities and the patient not desiring implant placement [31].
Advantages	Abundant vascularization of LD flap [2], [58]; Scars hidden by bra; No microsurgical expertise is needed [48]; Excellent tissue for coverage implant and its feasibility; Goods aesthetics results; Natural aspect.
Disadvantages	Muscle atrophy; Frequently need of implant and/ or tissue expander placement; Risk of seroma formation and rupture, displacement, contracture or infection implant; Risk of implant necrosis.
Complications	According to [94] 10% of local complications; <1% of flap loss; <1% of urinary tract infection; 20% of seroma; In addition to the complications associated with implants, transfer of LD carries a risk of seroma [7].

Gluteal and Thigh flaps

When the lower abdominal is not available as a donor site and patient prefer the use of autologous material, the gluteal area and thigh are the second choice for surgeons. If higher amount of volume is requiring the gluteal artery perforator is the best method to the breast reconstruction. Otherwise, if volume required is smaller and there is enough tissue available on the upper medial thigh a transverse upper gracilis flap is used.

GA-Gluteal Artery flap

This technique is similar to the DIEP and SIEA flaps because does not require the harvested of the muscle. When the superior gluteal artery is used as blood supplier, the flap is called by SGA and when the inferior gluteal artery is applied as blood supplier, the flap is called by IGA. The gluteal arteries are dissected to the internal iliac artery and exit the pelvis superior and inferior to the piriformis muscle, for SGA and IGA respectively. The superior gluteal artery enters the gluteus maximus muscle one-third of the distance along the line drawn between the posterior iliac spine and the greater trochanter (figure 2.2.12) [95].

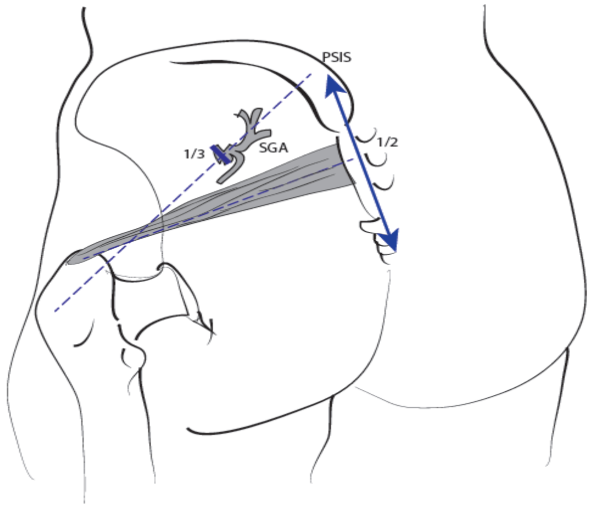


Figure 49. Superior gluteal artery (*SGA*) exits pelvis approximately one-third of the way along a line extending from the posterior superior iliac spine (*PSIS*) to the greater trochanter (*T*). (*Modified from Spear.*[96])

Figure 2.2.12: SGA flap anatomy [7].

The use of this option in breast reconstruction is indicated when the abdominal of patient is unavailable because the insufficient tissue or the presence of abdominal scars and patient's desire to stay with the scar in gluteal zone. According to Moore and Farrell [96], the IGA provides better aesthetic outcomes than SGA. Study conducted by Guerra *et al.* [97] refers that the gluteal artery perforator flaps are associated with decreased donor-site morbidity compared with musculocutaneous gluteal flaps and reports that 98% of overall gluteal artery flap survival and the partial flap necrosis occurred in 4% and seroma in 2%. Table 2.2.7 presents the characteristics of GA flap.

Table 2.2.7: Table of GA flap characterization

Flap Name	GA
Contraindications	History of previous liposuction at the donor-site and active smoking [7].
Advantages	Safe reconstructive procedure; Maximum preservation of gluteus maximus muscle; Pedicle provides sufficient length for a comfortable anastomosis.
Disadvantages	The necessary rearrangement of patient during surgery; The technical challenge of raising this flap; The potential risks of injury to the sciatic nerve or postoperative pain.
Complications	On average 6% present vascular complications; 2% total flap loss; 4% of patients require revisions because contour deformity [41], [81].

FCI- Fasciocutaneous Infragluteal flap

The FCI flap is other available alternative, for the situation that abdominal is precluded [91]. This technique is based on constant end artery of inferior gluteal artery with a safe location, good caliber and a long pedicle length. In thin patients with missing volume, this type of flap is an alternative for autologous breast reconstruction. The tissue from this site is more compact compared with lower abdominal flaps providing firm breast, important factor in younger patients.

2.2.3. Breast Reconstruction with Acellular Dermis

This type of reconstruction uses acellular dermis matrices in implant and expander- based breast reconstruction. The matrices are originated from human, porcine and bovine. The use of acellular dermis matrix, specially of human, is a good alternative in patients with high-risks because this procedure is less extensive resulting in a decrease of morbidity compared with others techniques [98] and used in patients with insufficient tissue to cover the implant [22]. This procedure is associated with a decreased of capsular contracture rate [99], [100], an improved tolerance to radiotherapy, and natural final aspect [33]. According to study by Gamboa-Bobadilla [98], 92% corresponds a successfully breast reconstruction. However, the same study reported several complications associated to this technique such as hematoma, infections and seromas.

2.2.4. Fat Graft based Breast Reconstruction

Autologous fat grafting (AFG) is used to refine and improve outcomes, and has become a popular tool in aesthetic and reconstructive breast surgery. This procedure uses the liposuction method for harvesting fat of the patient and after its reinjection into the defect site to be corrected. The donor site can be abdomen, medial, lateral or anterior thighs, lower back, knees, etc. According to Padoin *et al.* [101] the lower abdominal and medial thighs contain higher concentration of adipose-derived stem cells compared with fat from others donor sites. Each patient must have more than one donor site because the procedure takes four to six stages of fat grafting separated by periods of 3 months [102]. The AFG is an effective technique to correct irregularities from surgery, such as contour defects and volume asymmetries resulting of BCT. Although this procedure has become a popular tool, being a controversially method in surgeon's community, particularly in the presence of remaining glandular breast tissue after BCT. Graft fat with progenitor and stem cells have been associated with breast cancer progression [103]. But there is agreement on the fact that fat may not be injected into the glandular breast tissue. According to Kaoutzanis *et al.* [104] 60-70% of the injected fat is engrafted to the defect tissue and in 5% of cases occurs fat necrosis and oils cysts after AFG. However, there are not prospective studies of this procedure considering it completely safe [105], [106].

2.2.5. Timing of Breast Reconstruction Surgery

The breast reconstruction depends on reconstruction time point. According to Healy and Ramakrishnan [81], the reconstruction can be divided into 3 times: Immediate, delayed immediate and Delayed. The choice between immediate and delayed reconstruction is complex and needs to be studied by multidisciplinary aspects such as patient's choice, the need of postoperative radiotherapy, extent of the disease and other medical conditions [22]. The immediate breast reconstruction (IBR) occurs when the procedure starts at same time that mastectomy. The immediate-Delayed Autologous (IDEAL) breast reconstruction approach is a good alternative in case of Expander-Based Breast Reconstruction because expander implant is inserted temporarily and after adjuvant treatment is realized. The Delayed is option that starts any time after the adjuvant therapy has been applied. In study by Rogers and Allen [107] the patients who receive radiotherapy after DIEP flap reconstruction presented poorer outcomes than patients who do not undergo radiation after surgery. Furthermore, it was reported that immediate reconstruction exposed to radiotherapy increased rates of fat necrosis, fibrosis and contracture. Patients who have their breast reconstructed before their radiotherapy are exposed to increased late complication rates [108] and poor outcomes [107]. In case of radiation therapy after IBR the results may be compromised, namely patient with implant can develop capsular fibrosis and patient with flap, this can distort or shrink [27], [36]. Schaverien, Macmillan, and McCulley [109] revealed an increased risk of fat necrosis and a higher portion of revisional surgery after IBR and post mastectomy radiation therapy compared to delayed immediate reconstruction. The advantages and disadvantages of IBR and IDEAL approaches are presented in table 2.2.8.

Table 2.2.8: Table of timing reconstruction surgery characterization

Reconstruction Time	Immediate	Immediate-Delayed
Advantages	Preservation of the breast skin and inframammary fold resulting in better aesthetic outcomes than the delayed option [110], [111]; Minimization of social and psychological difficulties [22], better body-image, self-esteem and satisfaction [66], [91]; Reduction of total number of surgical procedures [112]; The associated costs are lower because fewer major operations are needed, the anesthesia is the same for the two interventions, the defect does not need to be recreated and the patients recover at the same time of mastectomy and breast reconstruction [113].	Best choice to maintain the balance between optimal aesthetic outcomes and effective radiation delivery [114]; Minimization of poor aesthetic outcomes (contracture, distortions); Revision of the inframammary fold [22].
Disadvantages	The uncertainty regarding radiotherapy and chemotherapy and their effects on breast reconstruction; Possible skin and nipple perfusion problems; The potential surgery complications of mastectomy and reconstruction accumulate due to prolonged surgery time; Longer hospitalization [22].	Increased of social and psychological difficulties; Treatment of patient is prolonged and elongated time of therapy; In case of autologous tissue reconstruction results poor outcomes due the skin envelope loss; Potential higher associated costs [22].

2.3. Imaging Technologies Used in Breast Reconstruction

2.3.1. Methods of Imaging Used in Pre-operative Phase

There are several imaging techniques used in planning breast reconstruction, but the choice is still a subject of discussion within the surgical community. Breast reconstruction planning includes the identification of the main perforator responsible for the blood supply of the flap allowing a reduction of the surgery time. This step is very important for the success of the surgery. The referenced methods of imaging in preoperative phase are computed tomographic angiography (CTA), magnetic resonance angiography (MRA), Doppler Ultrasonography, and dynamic infrared thermography (DIRT).

Computed Tomographic Angiography (CTA)

The CTA has been widely used in preoperative phase of breast reconstruction [70], [115]-[118]. In the last decade, the use of CTA has elaborated the 3D vascular architectural network and understanding of the microcirculation in the dermis with ultra-high resolution [115], [119]-[122] using a multi-slice Computerized Tomography, axial and coronal images [123]. Although, CTA does not provide physiological information on flow characteristics of perforators or assessment perfusion, the resulting images of CTA provide detailed information about source vessels, perforators, linking vessels and branching pattern within subcutaneous tissues and connection with adjacent perforator territories [124]. Thus, this information may allow the surgeon infers about the potential perfusion territories [125]. According to Smit *et al.* [126], the role of preoperative CTA allowed to determine through the caliber, course and characteristics of the perforator if a patient had suitable perforator. This preoperative information allowed the surgeon to develop a plan perforator selection. Also [127], [128], published data about the application preoperatively of CTA in perforator mapping of DIEP flap to examine perforator anatomy in terms of location, caliber and course. In the review of Casey *et al.* [129] was verified that most studies of CTA have sensitivity and specificity for perforator localization close to 100%. The use of preoperative CTA has had a beneficial effect on reducing operative time and increasing the number of suitable perforators to be included in a flap reducing the incidence of a postoperative abdominal bulge. This imaging technology requires a post-processing, volume rendering and 3D reconstruction following CTA, that allows an optimized and accurate visualization of vascular anatomy and course of the perforating branches which show high agreement with intraoperative findings [130]. The advantages and disadvantages of CTA are presented in table 2.3.1 and were extracted of table 1 of Mohan and Saint-Cyr [124].

Table 2.3.1: Advantages and disadvantages of CTA.

Imaging Modality	Advantages	Disadvantages
CTA	Considered gold standard; Fast image acquisition; Widely available; Can image larger BMI patients; Accurate localization and course of perforator; Can identify vessels down to 0.3 mm; Excellent spatial resolution; Easy interpretation with 2D and 3D reconstructions; Images can be reviewed independently; Eliminates inter-observer variability; Non-invasive; High reproducible; Short scanning time.	Ionization radiation exposure; Risk of hypersensitivity or nephrotoxicity; Need Contrast; Does not provide physiological information on flow characteristics.

Magnetic Resonance Angiography (MRA)

Magnetic Resonance Angiography (MRA) has been considered the next generation imaging technique of vascular anatomy [131]-[133], because of the imaging quality being enhanced without the aid of ionizing radiation, high contrast resolution, which can detect very small perforators allowing a better delineation of intramuscular course of perforators and in addiction high sensitivity (100%) [123], [132]. However, this type of imaging technology presents lower spatial resolution and Rozen *et al.* reported a low specificity (50%) when compared with CTA [134]. MRA provides images with high quality constituting an imaging tool which allows an accurate localization of perforators with high concordance with intraoperative findings [132], [133], [135], size, and distance from the umbilicus [123]. Chernyak *et al.* [132] and Vasile *et al.* [136] reported high correlation, approximately

97%, with intraoperative findings on assessment of dominant perforators using different flaps such as DIEP flap and gluteal and upper thigh flaps. Masia *et al.* [131] used MRA without contrast agents and obtained clear images of abdominal perforators. All dominant perforators of DIEP flaps used in breast reconstruction was identified and correlated with intraoperative findings. The use of contrast agents in MRA (CE-MRA) in examination of the DIEA vascular anatomy has been described by Chernyak *et al.* and Mathes and Neligan [132], [137] as considered the next generation in preoperative phase of DIEP flap. According to Schaverien *et al.* [135], the CE-MRA from their experience has a highly concordance between pre-surgical information from CE-MRA on the connections between perforator vena comitans and SIEV and the incidence of diffuse venous congestion [138]. Compared to iodinating contrast agent used in CTA, the CE-MRA with gadolinium has a better safety risk profile and lower hypersensibility [135]. Some advances in MRA include the newer contrast media such as extracellular gadobenate dimeglumine and newer blood pool contrast agents [139]. The limitations of MRA in preoperative planning for breast reconstruction are timing for examination, in detecting perforators less than 0,8mm in diameter, susceptibility to motion artifact, the higher costs compared to CTA, and the requirement for the patient to breath-hold for longer periods, which may not be feasible in some patients. Furthermore, it is considered not indicated in severe obesity, in patients with medical devices or foreign bodies and patients who cannot lay still or have severe anxiety or claustrophobia [139]. The advantages and disadvantages of MRA are presented in table 2.3.2 and were extracted of table 1 of Mohan and Saint-Cyr [124].

Table 2.3.2: Advantages and disadvantages of MRA.

Imaging Modality	Advantages	Disadvantages
MRA	Contrast agents may have safer risk profiles; No ionizing radiation; Arterial and venous image acquisition in single scan; Greater muscle to vessel contrast resolution; Easy interpretation of 2D and 3D reconstructions; Images can be reviewed independently.	Longer scan time; Need for MR contrast agent; Contraindications in patient with medical devices and claustrophobia.

Doppler Ultrasonography (Doppler US)

"The handheld Doppler device is a non-invasive method to measure the microcirculatory blood flow in, for example, the skin, based on the fact that the light impinging any moving scattering object undergoes a very small frequency shift, so-called Doppler effect" [10]. The Doppler instrument has two piezoelectric crystals in a cylinder. One of crystals emits continuous ultrasound at a constant frequency, while the other is a receiver. Ultrasound signal transmitted into a blood vessel is reflected by the blood cells and registered by the receiver crystal. Due to movement of the blood vessels, the reflected signal has a slightly different frequency than the transmitted signal according to the Doppler Effect [140]. Doppler Ultrasonography was the first method used by surgeons for preoperative mapping perforating vessels throughout the cutaneous territory of a flap. The use of handheld Doppler and color duplex ultrasonography have been traditionally used in detection of the location of perforators and flow characteristics [141]-[144]. Useful information about the location, caliber and flow patterns of perforators in the preoperative phase of the TRAM flap using color Doppler has been widely studied [70], [141]-[144]. The resulting images using Doppler ultrasonography provides easily details about flow, direction, velocity and this imaging could differentiate between venous and arterial signals. Giunta, Geisweid, and Feller [144] reported on the usefulness of handheld Doppler for preoperative localization of perforating vessels and showed a relatively high number of false positives results (47,6%), to the relative high sensitivity of the method and the detection was found to be 96% effective. The authors found good relationship between pre- and intraoperative findings with an average distance of 8 mm between preoperative measurements of the arterial Doppler sounds and intraoperative measurements of the real perforators. Although, Doppler ultrasonography is a clinically useful monitoring method, it has limitations such as the risk of dislocation of the device when applied, operator dependency, significant inter-observer variability, high false positive rates, and only provides a 2D picture of the underlying architecture [126]. Despite this, equipment may be too sensitive and can detect perforators that are in fact too small to be used for perforator flap surgery. The advantages and disadvantages of Doppler US are presented in table 2.3.3.

Table 2.3.3: Advantages and disadvantages of Doppler US.

Imaging Modality	Advantages	Disadvantages
Doppler US	Information about location, caliber, flow patterns, direction and velocity of perforators easily determine; Differentiation between venous and arterial signals.	Risk of dislocation of the device; Significant inter-observer variability; Conducted over 45-60 minutes by highly experienced personnel; High false positive rates; Difficulty in interpretation of findings; Only provides a 2D picture of the underlying architecture.

Thermography (TG)

The infrared image is based on detection of natural thermal radiation emitted by an object surface such as the human skin in medicine and the interpretation of temperature distributions in terms of physiological alterations [145]. The thermography and specifically the dynamic infrared thermography (DIRT) have been used in preoperative perforator selection in breast reconstruction. In addition, its application in the preoperative phase, the DIRT has also been applied in the intra and postoperatively. The results can be validated with Doppler Ultrasonography to ensure accuracy. In this dissertation, the DIRT (a thermography strand) will be extensively studied in the three phases of breast reconstruction and for a better understanding, the basic principles of the thermography technique and its application are described in detail in sections 2.5 and 2.6, respectively. The advantages and disadvantages of TG are presented in table 2.3.4.

Table 2.3.4: Advantages and disadvantages of TG.

Imaging Modality	Advantages	Disadvantages
TG	Non-invasive; Non-ionizing; No requires contrast agents; Simple; Rapid examination; Low patient risk profile; Low cost;	Limited to 2D map; Provide skin surface information; Requires control environment; Requires preparation of individual; Variable data; Moderate Accuracy.

Comparison of the Different Imaging Technologies for Planning Breast Reconstruction

CTA has superseded Doppler Ultrasound (US) in many medical institutions, but it is not considered the first choice in preoperative imaging [146], [147]. CTA in study of Rozen and colleagues [148] was superior because presented a clear visualization of the DIEA, its branching pattern and the perforators when compared with Doppler. Cina *et al.* [147] reported that both modalities CTA and Color Doppler US were accurate in perforator mapping and had their associated strengths and weakness in assessing artery calibers and estimating the intramuscular courses. Their results showed an accuracy of 97 % for color Doppler and 91 % for CT angiography in identifying perforator arteries. Due to the cost and radiation dose of CT angiography, these authors recommend using color Doppler as first choice and supplying with CT when the results of color Doppler examination are inconclusive. On the other hand, there are controversial studies of Doppler US and CTA in terms of determining the superiority of perforator location of one modality over another [148], [149]. Although CTA presents higher cost than ultrasonography, it is still considered as affordable and currently than MRA method.

The studies report a good outcomes using thermography and laser Doppler US [150].

MRA modality presents some drawbacks when compared to CTA including the high costs, in detecting perforators less than 0,8mm in diameter, susceptibility to motion artifact that can affect visualization and low spatial resolution. But, as advantages presents greater contrast resolution and does not need ionizing radiation.

The table 2.3.5 was extracted of [123] where is presented a comparison of the various tools for assessing the characteristics of the source and perforating vessels and the costs and availability of different techniques used preoperatively.

Table 2.3.5: Comparison of the various tools for assessing the characteristics of the source and perforating vessels.

Method	Radiation Exposure	Contrast	Caliber	Location	Flow	Availability	Cost	Accuracy
Doppler	No	No	No	Yes	No	High	Medium	Low
Color Duplex	No	No	No	Yes	Yes	Medium	Medium	Moderate
CTA	Yes	Yes	Yes	Yes	No	Medium	High	High
MRA	No	Yes	Yes	Yes	No	Low	High	High
TG	No	No	No	Yes	Yes	Low	Low	Moderate

2.3.2. Methods of Imaging Used in Intraoperative Phase

Following the preoperative mapping, the next step is to assess the perfusion of the flaps based on the primary blood supply. This perfusion has been assessed through observing the color of the flap and determining the rate of capillary refill in the center and at the periphery of the flap. In addition to DIRT for intraoperative assessment, there is a method that allows direct visualization of perfusion within a cutaneous territory, called Fluorescent Angiography.

Laser-assisted indocyanine green fluorescence angiography (LA-ICGFA)

The LA-ICGFA needs to inject the indocyanine green (ICG) intravenously for to capture cutaneous vascularity within 15 seconds to 2.5 minutes using infrared energy to excite the ICG. The device contains incorporated video and is linked to a computer that has a software of analysis to generate quantitative data providing image [139]. The images can be captured before flap elevation, during flap elevation, after flap elevation and postoperative phase. The LA-ICGFA allows characterize flow and perfusion in flaps and tissue and its use has focused on intraoperative assessment [151], [152]. This modality of imaging is considered better at assessing flap physiology and perfusion used intra-operatively as an adjunct to clinical verdict allied to another preoperative imaging technology to improve predictability and reduced complications in reconstruction. There are many studies that report the extensive use and success of this imaging technology in autologous breast reconstruction confirming the viability of the mastectomy skin flaps [151]–[154].

2.3.3. Methods of Imaging Used in Postoperative Phase

There are many methods used in postoperative assessment such as handheld Doppler, DIRT, surface temperature, flap turgor, capillary refill and flap color [155]. But these last methods are dependent of subjective interpretation of clinical personnel becoming a limited method although can be effective. In postoperative, during to 2 hours, is important to detect different problems for allows to save flap avoiding the flap necrosis. If there are inflow problems the flap becomes pale, cool, and soft with delayed or absent capillary refill. On the other hand, if there are venous outflow problems the flap becomes tense, congested, and purple, with brisk capillary refill.

Near Infrared (NIR) Imaging

Near infrared imaging is a method that allows the continuous monitoring of oxygen saturation within the cutaneous layer of flap. The probe is placed on the skin emitting near infrared light and permits detect the hemoglobin content in the vessels. This probe is linked to computer that generate the data. Any alteration in arterial or venous flow is detected immediately. Keller [156] used this modality in all patients and in case of abnormal flap perfusion all were saved.

2.4. Thermography

The main information provided by thermography is the absolute value of temperature and its distribution in skin surface. The first medical application of thermography was in 1956, by Ray Lawson, through the usage of an evaporograph system to look at temperature distribution of a breast cancer malignant tumor tissue [157]. It is a non-invasive and non-ionizing technique, the measurement of temperature is based on the frequency distribution of temperature of a black body, detailed in more detail at this section of the document.

2.4.1. Thermal Physics

The electromagnetic spectrum presented in figure 2.4.1 is the set of all possible frequencies of electromagnetic radiation emitted or absorbed by specific object in determinate wavelength. The objects with temperature over absolute zero have the ability to emit thermal radiation. A black body is a physical imaginary object, which have the ability to absorb all the incident total electromagnetic radiation regardless of frequency or angle of incidence, with the capacity of emitting only thermal radiation at a specific designated wavelength (emissivity = 1) [158]. The surface of human skin, is an efficient radiator closer to the perfect black body where emissivity (ratio between the ability of human skin and a blackbody emitting thermal radiation) value is 0.98.

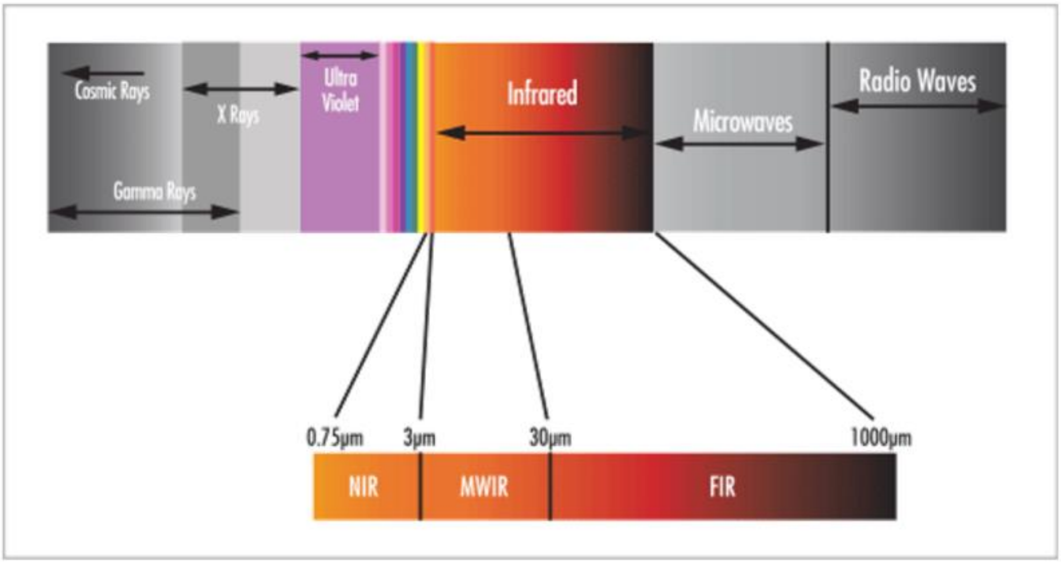


Figure 2.4.1: Representation of Electromagnetic Spectrum [159].

The emissivity of an object is an important factor in temperature measurement, since it represents the aptitude of an object surface to radiate thermal energy, which depends on its texture and color. The radiation emitted from a blackbody can be described by three expressions: Planck's radiation law, Wien's displacement and Stefan-Boltzmann (equation (2.4.1)). Plank's law describes the spectral shape of the source as a function of wavelength and it shows that human skin emits infrared radiation mainly in the wavelength range of 2-20μm with an average peak of 9-10μm. On average, 90% of the emitted infrared radiation in humans is between 8-15μm.

The Wien's displacement law exemplifies how the spectrum of blackbody, at any temperature, is related to the spectrum at any other temperature. Finally, the Stefan-Boltzmann equation provides the amount of energy emitted by a blackbody of a specific spectral unit (wavelength, frequency or wavenumber), and through the comparison of the perceived radiation value with this reference, a temperature value is obtained [157], [160].

$$E_b = \varepsilon \, \sigma T^4 \qquad (2.4.1)$$

The amount of radiated electromagnetic energy of an object is directly related to its temperature. An object can be characterized by its capacity of absorbing or emitting electromagnetic radiation [161].

The thermography is a complementary diagnostic tool, being non-invasive, non-ionizing, fast, relatively simple and able to monitor a significant superficial area of interest in real time. This technique does not produce any adverse effects [162], becoming a good method in clinical field for to characterize and detect physiological changes through skin temperature, reflecting the microcirculation, autonomic nervous and musculoskeletal systems [163]. Each pixel of image produced by thermal camera corresponds to a temperature value, being subject by a false color scale to a subjective interpretation [164].

2.4.2. Thermal Physiology-Thermoregulation

The body core temperature is an essential factor to preserve homeostasis, which is one of the main functions of human body, allowing to maintain its integrity and composition of body fluids and tissues. Significant changes in the core temperature outside of normal range (35.5 to 37.7ºC) is a clear indication of a physical dysfunction and temperature changes outside this range may disrupt the essential chemical processes within the body and lead to severe consequences [165]. Thus, the thermoregulation plays the vital role in maintenance of human life and it is described as a set of mechanisms which permits to regulate body core temperature. This ability to maintain and regulate the core body temperature happens in a narrow range of values when there are changes from extern environment. In humans the body core temperature reaches approximately 35.5◦ C in morning and 37.7◦ C in evening [157]. However, these values are generalized and may vary from person to person and this variation is directly dependent on physiological and environmental factors such as age, sex, body mass index, menstrual cycle, and others [166].

The body core temperature is controlled by hypothalamus, an organ located in interior of cranial cavity, acting as the center of thermal regulation. This system makes the balance between heat production and heat loss, working as a negative feedback circuit. The hypothalamus is informed of external changes in temperature through thermoreceptors located in skin surface and detects internal variations of temperature through the monitoring of blood temperature. The thermoreceptors together with the autonomic nervous system, activate mechanisms of heat loss, when is perceived a high temperature, or activate mechanisms of heat production in case of the lower temperature recognition [145], [160]. The anterior hypothalamus is responsible for reflex responses that allow to keep the body core temperature constant. When a warm environment is perceived, the hypothalamus sends neuronal signals for activation of heat loss methods such as the increase in the transpiration rate, vasodilation and reduction of metabolic rate. The posterior region of hypothalamus is responsible for responses in cold situations through of heat production and losses reductions mechanisms, the vasoconstriction, tremors and erection of skin hairs [167].

2.4.3. Heat Transfer Processes

There are four physics mechanisms of thermal energy transfer from the human body to the external environment [166] and are represented in figure 2.4.2:

- **Conduction**: the heat is dissipated by direct contact, from the skin to solid objects. 3% of body heat is dissipated through this mechanism in a steady state [166].
- **Convection:** the thermal energy is transferred through a fluid, gas or liquid, such as bloodstream and urine. 15% of body heat is dissipated by this mean in a steady state [166].

- **Radiation:** Occurs spontaneously when the heat is liberated through infrared waves in electromagnetic spectrum [157], [168]. Around 60% of body heat is dissipated by this process in a steady state [166].
- **Evaporation**: Occurs when the thermal energy is dissipated by the sweating glands, liberating water to the skin, for cooling it, being transformed into a gas through vaporization, which is evaporated to the surround air [157], [168]. 22% of body heat is dissipated by this mechanism in a steady state [166].

The human body executes heat changes with environment as a part of normal thermoregulatory process, most of these heat changes occur by radiation, which can be registered by electronic thermal imaging [169].

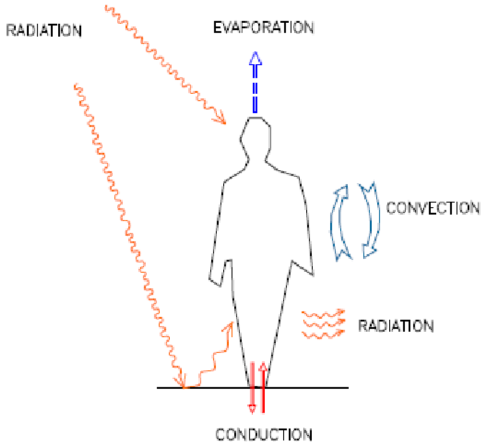


Figure 2.4.2: – Representation of thermic energy transfer processes [170].

2.4.4. Standardization of Thermography

In order to thermal images produced by infrared imaging being considerable reliable and its results reproducible, it is necessary to follow established guidelines [171]. This standardization presents numerous advantages such as: repeatability, ease of understanding and knowledge exchange, reduces the influence of variables, etc. This is the only way to eliminate errors of the past due to the lack of use of standards in registration of images, and greatly enhance the credibility of the technique and consequently widely its use in medicine [172], [173]. In 1974 the European Association of Thermology created guidelines for the good practice of the technique [174]. These standards are based mainly on the requirements of patient preparation, conditions for thermal image and criteria of the use of this kind of images in medicine [166], [175]. Two very important factors that have a strong impact on the data subsequently obtained are: the camera quality and the ability and skill to operate the camera. The incorrect use of camera and the failure in practice of guidelines has caused disagreement in the area. There are rigid protocols in thermography use namely in medical field, which plays a crucial role in reliable practice of this technique. A recent ISO standard called "Particular requirements for the basic safety and essential performance of screening thermographs for human febrile temperature screening" IEC80601-2-59 [176] provides performance requirements, calibration and good practices in the use of the thermal camera. The appropriate number of pixels in the area of registration of temperature is an important factor to take into account when using this device [175].

The internationally accepted standards [177], [171], [178] includes a period of preparation and thermal stabilization of the patient, to reduce the influence of the environmental conditions of the room where the examination is performed on the results obtained. In Europe, the room temperature should be between the 18° C and 24° C, the relative humidity should be less than 50%, the patient must be in the room at least 10 to 15 minutes prior to performing the examination to the body adapt to room conditions. If the patient ate a heavy meal, drank alcohol or any hot drink, used ointments and consumed drugs or medicines the results will be influenced by these factors [157]. The use of an inappropriate image system with the required quality will affect the process and the quality of the data acquired. There is a huge concern in standardization for all these variables are taken into account to homogenize the data to allow later compare them with reference data [179].

2.4.5. Limitations of Thermography

The mains limitations of infrared thermography are: only provides information about the skin temperature, the interpretation of images requires experience and are dependent on the sensibility and expertise of operator, it is hard to capture images in external environments due to sun reflection, the patient cooperation dependency and the requirement of a controlled environment [177].

2.4.6. Static Infrared Thermography

In static infrared thermography, single images are taken without exposure of the area of interest to an external stimulation before to image acquisition. The interpretation of static thermograms mainly depends on the identification of asymmetric temperature distribution and single measurements.

2.4.7. Dynamic Infrared Thermography

The static infrared imaging presents an extensive set of attractive characteristics for practical applications in medicine field, such as no contact with patient, simple data acquisition and portability. However, it presents limitations due to the fact of measured absolute values of temperature not always be accurate and valid due to the accuracy of capturing instruments and the effect of circadian cycle [180]. Thus, there is a need to use dynamic thermal imaging for evaluating the temperature evolution over time and characterize the behaviors applying external stimulators sources, which can be chemical, thermal or mechanical. The temperature challenge is widely used and consists of either cooling or heating, may be achieved with cooling fan, water immersion, application of a aluminium plate on the skin or any other technique that provides a uniformly distributed temperature change to the tissues. Generally, the dynamic infrared thermography (DIRT) is based on stimulation through an external energy and observation of thermal response. DIRT is considered as a technique straightforward. When a thermal stimulation is applied, in case of surface cooling, it causes a relative hypoperfusion of the cutaneous surface. After termination of the cold challenge, the tissues rewarm. Thus, during DIRT examination, differences in the rate and pattern of rewarming became apparent.

2.5. Use of DIRT in Pre, Intra and Postoperative Phase of Breast Reconstruction

The autologous breast reconstruction is seen as the preferable choice for most patients, but the procedure is perceived to be more complex, technically more challenging, has longer operative time, recovery time, and higher earlier complication risk [124]. The inadequate perfusion is considered the main cause of flap loss, which constitutes one of the most common complications in breast surgery. Thus, for successful surgery, the surgeon needs to have all the detailed information about the anatomy and physiology of the cutaneous circulation of the flap. The use of thermal imaging allows assessing the cutaneous circulation monitoring of the flaps without radiation or intravenous contrast medium for examination. The DIRT (Dynamic Infrared Thermography) technique uses an infrared camera, which allow obtain a map based on the heat from the deeper warmer tissue to the skin surface [181]. The perforator blood vessels can be visible as hot spots [182]. The DIRT technique is an interesting tool for breast reconstruction, namely in the pre-operative, intra-operative and post-operative phases. The use of DIRT as an important and positive method that provides a qualitative assessment of perforators and valuable information that helps in planning and designing the flaps, in pre-, intra- and post-operative phase of breast reconstruction [10], [74], [183], [184].

2.5.1. Use of DIRT in Pre-operative Phase

The pre-operative imaging allows an accurate identification of perforators and a qualitative assessment facilitating the preoperative decision. The dissection of flap is a complex procedure with error limitation and the knowledge of the location of dominant perforators, which will be used to perfuse the flap at target, is an important issue in autologous breast reconstruction. This role in preoperative phase can assist the surgeon in exploring or confirming flap choices based on presence of suitable perforators. At this point, it is necessary to identify, locate and map the perforators, in order to reduce future complications and operating time, optimizes flap design and obtains a successful operation and outcomes [70], [185], [186]. The use of the DIRT in this operative phase has been widely studied. In this procedure is applied a thermal challenge over the flap and after this stimulation the rate and pattern of rewarming is continuously monitored with the infrared camera. Analysis of rate and pattern of rewarming of hot spots contributes to the easy identification of the most powerful perfused perforator to be selected. The perforators were clearly detected and identified using DIRT in the studies by Zetterman *et al.* [150] and Salmi, Tukiainen, and Asko-Seljavaara [184]. In the first study was used a COLDI-micro thermocushions as a method of thermal stimulation in abdominal flaps during to 30 and 300 seconds and after the cooling, the hot spots were more readily visible than at room temperature. Longer cooling time provided a 3.4 times better contrast and a longer visibility of the hot spots compared to the shorter cooling time. In the study of Theuvenet *et al.* [187] 31 out of 36 perforators were located by DIRT that has been used since 1983 in high risk patient and proved to be an efficient method. According to Weerd, Mercer, and Weum [9], who used DIRT, the dominant perforator was correctly identified by preoperative thermography in all cases. Other study performed by Weerd and colleagues studied the use of DIRT in 23 patients using DIEP flap and in 4 patients with SIEA flap. A desktop fan was used to deliver the cold challenge by blowing air at room temperature over the abdomen for a period of 2 minutes. The thermal images were taken of the abdomen in the supine position, same position of operation (90°). In 23 patients was used DIEP flap and the location of suitable perforator was well selected by DIRT because the perforator selected was well associated in intraoperative phase and there was a complete correspondence between DIRT and multidetector computer tomography scan (MDCT) examination [188]. These authors affirms that there is a positive relation between the brightness of the hot spot and the auditive Doppler volume and after have carried out many studies comparing DIRT with different techniques for preoperative planning such as Doppler ultrasound flowmetry and MDCT, they stated that DIRT is a reliable technique for identifying suitable perforators [189]. Muntean *et al.* [181] performed a trial in pigs using DIRT. After pulverizing alcohol in region of study, a fan was used to deliver air at room temperature for 60 seconds as method of thermal stimulation. This study showed that the dominant perforator was exactly identified with surgical findings through the CDU and DIRT in all cases. In all perforators detected in MDCT scans there was a clearly relation to perforators selected with DIRT [10]. Other study performed by Whitaker *et al.* [190] also described the usefulness of thermography in pedicled perforator. According to Mercer *et al.*, that performed a dynamic study using thermography with blowing air at room temperature over the abdomen for a period of 2 minute using a desk top fan, a good choice of a suitable perforator in preoperative needs to fulfil the following criteria [10]:

1. A rapidly appearing hot spot after the cold challenge;
2. This hot spot is associated with an audible Doppler sound;
3. The perforator is not located at the edge of the flap.

Summarizing, the DIRT is used pre-operatively to help to more clearly identify vascular circulation of flap. Tenorio *et al.* [191] performed a study comparing DIRT with handheld Doppler on 16 patients with surgical dissection to confirm location of perforator as a reference standard. This trial showed that location matched within a distance of 0-15 mm in 67% patients and they concluded that Doppler located perforators in the deeper level, where they exited the muscular fascia and thermography detected their location beneath the skin and hence both methods were complementary. In table 2.5.1 are presented the methods used by different studies in preoperative phase of breast reconstruction using DIRT.

Table 2.5.1: Table of preoperative study characterization using DIRT.

Study	Weerd, Weum and Mercer**[188]**	Weerd, Mercer, and Setså **[183]**	Weerd, Miland and Mercer **[74]**	Whitaker et al. **[192]**
Acclimatization time	5 minutes	20 minutes	10 minutes	n.a.
Method of thermal challenge	Blowing air with desktop fan	Blowing air with desktop fan	Blowing air with desktop fan	Water pack at 5ºC
Time of challenge	2 minutes	2 minutes	2 minutes	10 minutes
Day of study	Immediately before surgery	On preoperative day	On preoperative day	n.a.
Complementary imaging method	Handheld Doppler	Handheld Doppler	Handheld Doppler	CTA
Time of recovery (minutes)	5 minutes	n.a.	n.a.	n.a
Phases of data collections	A, B, C, D, E, F, G, H	A, B, C, D, E, F, G, H	A, B, C, D, E, F G, H	n.a.

Phase	Definition
A	Initial photo of flap design with the location of arterial Doppler sounds marked;
B	IR thermal image prior to cooling;
C	IR thermal image at end of thermal challenge;
D	IR thermal image at 1 minute after thermal challenge;
E	IR thermal image at 2 minutes after thermal challenge;
f	IR thermal image at 3 minutes after thermal challenge;
g	IR thermal image at 4 minutes after thermal challenge;
H	IR thermal image at 5 minutes after thermal challenge.

2.5.2. Use of DIRT in Intra-operative Phase

Studies [193]-[195] affirmed that failure of free flaps occurs during operative time rather than postoperative phase. Thus, in the intraoperative phase is important to monitor the blood circulation state of the flap. Monitoring free flaps may keep the time interval between the onset of ischemia and its recognition as short as possible and therefore improve successful rates. DIRT plays a key role in this phase because provides in real time indirect vital information to surgeon for flap survival. DIRT can detect dynamic changes in flap confirming the integrity vascular of pedicle after dissection or after the flap has been inset in defect site [9]. When the flap is harvested from the donor site, there is no blood supply for a period of time that can extend in one hour before to be reconnected to the mammary vessels in thoracic wall. At this time the temperature of flap decreases. Through DIRT, when surgeon completed microsurgical reconnection, is possible observe and quantify objectively the rate and change thermal pattern of rewarming thermal dynamic process, this mean that, is possible to see the appearance of a hot spots indicating early rewarming [10]. The rapid appearance of hot spots on the flap and a general rewarming of the entire flap are expected to a successful microsurgical reconnection and the breast surgery construct [183]. However, if these hot spots do not appear, it is a sign of the inappropriate establishment of blood supply, partial or total obstruction of arterial inflow result of, for instance, twirl or external compression of the feeding vessels. After this step, the flap is physically manipulated to obtain the correct breast form and this procedure constitutes a risk of damaging or compromising the blood circulation of flap so is important continuously monitor temperature of the flap [10]. In the study by Weerd, Mercer, and Setså [183] the use of DIRT, through thermal stimulation with metal plates, for intraoperative monitoring reperfusion of DIEP and SIEAP proved to be a successful and safe technique. This is possible, due to its use in the intraoperative phase registered successful arterial flow and partial or total obstruction of arterial inflow, which is difficult to detect, allowing to save the flaps. In this study, there were observed some complications during the operation. In 2 flaps the rate of skin rewarming was low and the appearance of hot spots was less evident in thermograms. Clinical examination of the flap was indicative for poor flap perfusion. In one patient, the pedicle twist was the cause of the complication and after the pedicle had been repositioned, the rate and pattern of rewarming improved dramatically confirmed by clinical evaluation improvement reperfusion. In the other, a surgical instrument exercised external compression over the pedicle resulting in a poorly flap perfusion. Removal of the instrument caused the rapid appearance of well-defined hot spot in thermal images.

Summing up, if circulation of the flap is affected this phenomenon is visible in the thermal images and allows the surgeon to quickly intervene and correct the defect in perfusion flap [196]. Mercer *et al.* [10] mentioned that to test the adequate re-established blood supply after initial procedure, various stages during modeling process and at end of the operation, was applied cold challenges tests either by lightly applying a cool metal plate to the skin for a few seconds or simply by washing the flap with physiological saline solution at room temperature. Both methods cause a skin cooling, which if blood perfusion is adequate, is followed by appearance of hot spots as the flap rewarms. Nevertheless, other study performed by Theuvenet, Koeyers, and Borghouts [186], reports that thermography is an available technique for monitor other types of autologous flaps. In table 2.5.2 are presented the methods used in intraoperative phase of breast reconstruction using DIRT.

Table 2.5.2: Table of intraoperative study characterization using DIRT.

Study	Method of thermal challenge	Time of challenge	Time of Recovery	Phases of data collections
Weerd, Mercer, and Setså **[183]**	Metal plate	Few seconds	3 minutes	A, B, C, D, E, F, G, H, I, J, K, L, M, N
Weerd, Miland, and Mercer **[74]**	n.a.	n.a.	n.a.	H-K

Phase	Definition
A	Digital photograph of a free flap at the donor site;
B	IR thermal image of a free flap at the donor site;
C	Digital photograph of flap;
D	IR thermal image just before clamp release;
E	IR thermal image taken at the moment of clamp release after completion of microsurgical anastomosis;
F	IR thermal image taken 2 minutes after of clamp release after completion of microsurgical anastomosis;
G	IR thermal image taken 4 minutes after of clamp release after completion of microsurgical anastomosis;
H	IR thermal image taken prior to the cooling after a successful anastomosis to the mammary vessels;
I	IR thermal image taken 1 minute after the thermal stimulation at the end of a successful anastomosis to the mammary vessels;
J	IR thermal image taken 2 minute after the thermal stimulation at the end of a successful anastomosis to the mammary vessels;
K	IR thermal image taken 3 minute after the thermal stimulation at the end of a successful anastomosis to the mammary vessels;
L	IR thermal image taken some minutes after an extra venous anastomosis;
M	IR thermal image taken in case of pedicle compression;
N	IR thermal image taken after the relief of the compression.

Note that in the review of some studies using DIRT in pre, intra and postoperative performed by Mercer, Weerd, Miland and Weum [10] is referred the washing the flap with physiologic saline solution at room temperature as a cooling method used in intraoperative phase of breast reconstruction.

2.5.3. Use of DIRT in Post-operative Phase

DIRT has been shown to be a reliable technique to monitor flap perfusion in postoperative phase to ensure the adequate perfusion in the new breast and allows detect complications in ligation between perforators of flaps and mammary internal vessels [10]. In study performed by Weerd, Miland, and Mercer [74] breast reconstruction was carried out in 16 patients. The flaps were monitored by clinical assessment such as color, refill, turgor, and temperature and by arterial perforator sounds using handheld Doppler and DIRT with thermal stimulation by blowing air for 2 minutes in first, third and sixth postoperative days. This study reported that a week after surgery, healing is a dynamic process, and it can be monitored with thermal imaging, its thermal activity is expected to be increasing over time. There was a clear improvement of blood perfusion from the first to the sixth day, with a skin temperature increasing. The DIRT constitutes extra reassurance of perfusion flap from the next days after surgery to up six months. As described above there is a high risk of complications in the postsurgical phase associated to breast reconstruction. The partial necrosis of flap edges and total necrosis are the most common. These problems have some consequences such as long hospitalization, increased risk of surgical site infection, necessity for subsequent operations, increased costs of treatment, and finally a poorer aesthetic and functional outcome. Despite the well-researched anatomy of flaps, namely TRAM flap, complications continue to occur developing the partial flap necrosis due to inadequate blood perfusion [11]. Through the application of the thermography in monitoring postoperatively of vascular perfusion, it was possible to detect a possible decrease in flap temperature in a short period of time indicating the absence of patency in microsurgical anastomoses constituting a warning to a new surgical procedure [198]. In the study of Kołacz, M. Moderhak, and J. Jankau [11] were observed 9 marginal necrosis of flap in 38 patients and no flap developed total necrosis. In this paper is showed images and thermograms of one patient who had necrosis. In this patient is visible signs of impaired flap perfusion such as skin color and capillary refill time in a simultaneous clinical evaluation as late as after 24 hours and persisted until day 7. In the thermogram corresponding to day 7 after surgery, it is possible to see that the mammary area where the flap is located has a lower temperature than the zone surrounding the breast indicating the inadequate perfusion of the flap. The analysis of thermogram and clinical examination allowed the identification of necrosis at the edges of flap used in breast construction. At 7 days after surgery, the necrotic tissue was removed and the thermogram of day 21 after surgical procedure shows an increase of the flap temperature compared to the previous thermogram indicating its adequate blood perfusion. In table 2.5.3 are presented the methods used in postoperative phase of breast reconstruction using DIRT.

Table 2.5.3: Table of postoperatively study characterization using DIRT.

Study	Acclimatization time	Method of thermal challenge	Time of challenge	Time of collections	Complementary Methods	Phases of data collections
Weerd, Miland, and Mercer **[74]**	10 minutes	Blowing air with desktop fan	2 minutes	1,3,6 postoperative days	Clinical evaluation, handheld Doppler	A, B, C, D, E, F, G, H

Phase	Definition
A	Initial photo of flap design with the location of arterial Doppler sounds marked;
B	IR thermal image pre-cooling on day 1, 3, 6 after the operation;
C	IR thermal image end-cooling on day 1, 3, 6 after the operation;
D	IR thermal image taken after 60 seconds rewarming on day 1, 3, 6 after the operation;
E	IR thermal image taken after 180 seconds rewarming on day 1, 3, 6 after the operation;
F	IR thermal image taken after 240 seconds rewarming on day 1, 3, 6 after the operation;
G	In case of partial flap necrosis, digital photograph was taken on day 24;
H	In case of partial flap necrosis, IR thermal image was taken on day 24 after 65 seconds rewarming.

2.6. Burns

Infrared thermography has become a method increasingly used to adjunct more expensive and/or invasive investigations in a range of surgical fields. The combination of functional assessment, flow characteristics and anatomical localization has led to increasing applications of this technology in several areas of plastic and reconstructive surgery. One of these areas is the burns with purpose of evaluating the depth and deciding the more appropriate treatment. In this section, will be discussed the way of burns assessment with thermography and the main studies performed in this field.

2.6.1. Fundamentals of Skin

The skin is the largest organ of human body and is the interface between the body and the external environment. This system is constituted by hypodermis, skin that include dermis and epidermis and the structures attached such as hair, nails and glands (figure 2.6.1). The main functions of the skin are [165]:

- Protect the body from bacteria or foreign substances and from trauma to structures like veins, arteries and nerves;
- Contribute to the regulation of body temperature not only by radiation, conduction and convection heat but also through sweat production;
- Check sensory perception for touch, temperature and pain;
- Contribute to the production of vitamin D3 by exposure to UV radiation;
- Excrete small amounts of urea, uric acid and ammonia.

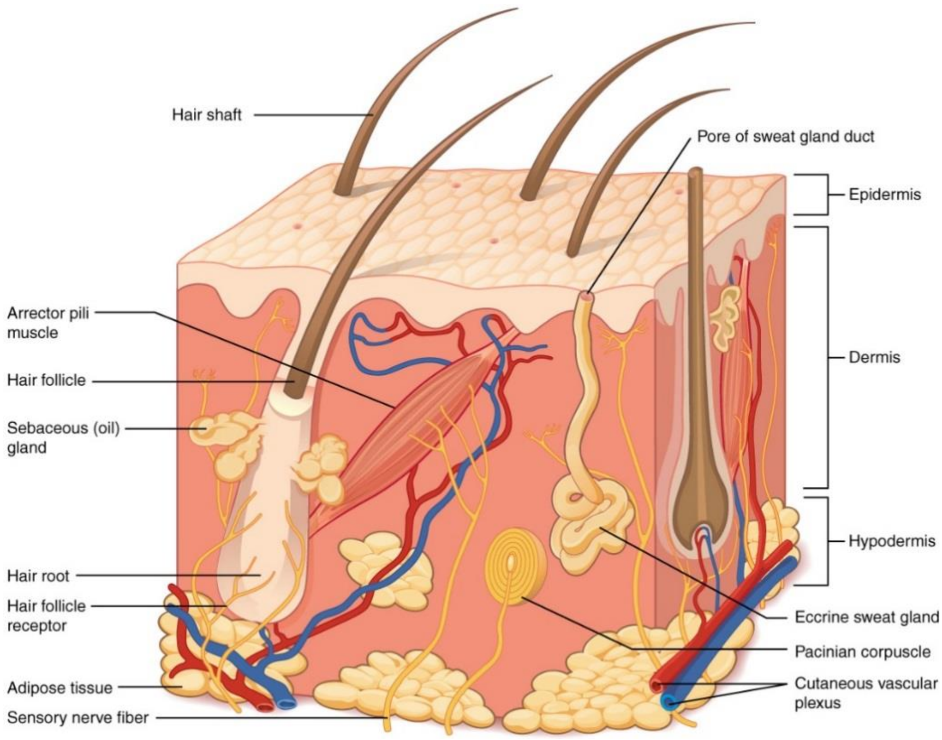


Figure 2.6.1: Structure of the skin.

The skin is constituted by two layers that are divided by a basement membrane. The first layer, epidermis is the superficial layer with approximately 0.1 to 0.2 mm of thickness [199] and is constituted by epithelium tissue. The epidermis not contain blood vessels and there are several types of cells: Keratinocytes which have to produce the keratin. The keratin is essential for structural resistance and impermeability to the water; melanocytes which produce melanin, responsible for skin colour and is the protection of UV radiation; Langerhans cells which are a part of immunity system and ensure the cutaneous immune vigilance; Merkel cells are associated to nerve endings which detect the tact function and superficial pressure. The other layer of the skin corresponds to dermis and is constituted by conjunctive tissue and it is above the hypodermis. In the dermis, there are nerve endings, muscles, blood and lymphatic vessels, hair follicles and the sweat and sebaceous glands. The dermis is divided into sub layers: reticular and papillary layers. The hypodermis is a region provided by nerves and is vascularized formed by loose conjunctive tissue. The major cells are fibroblasts, adipose cells and macrophages.

2.6.2. Burns Classification

The burns are a type of cutaneous wounds that can be classified according to the body superficial extension and the depth of affected skin area. The determination of extension depends on the age of patient and is evaluate through the “nine rules” (Wallace), a rule that divide the body in segments and is attributed to each body area a percentage equal to 9% (or multiple). The classification of burn depth is made by affected skin thickness.

Burns are caused by one of many types of interactions of tissue with:

- High temperature sources such as flames, hot solids, and liquids;
- Electrical energy dissipation;
- High energy ionizing radiation such as X-ray, nuclear, and UV radiation;
- Chemical substances such as acids, bases, and gas warfare agents;

All burns have specific character of injury followed by a healing process. The stage (depth) of an injury depends on a specific phenomenon and may be developed in time especially concerns chemical or irradiation lesions [200].

The accurate assessment of burn wound depth is an important determinant in treatment decision of the burned patient, especially in the case of a severe burn as the thorough evaluation enables the appropriate choice of treatment.

There are different ways to classify burn wounds. In clinical practice the burns are divided into [200]:

- **First degree (I°)** – **superficial** – only epidermis is affected. Vasodilatation of sub-papillary vessels in the burned area and the reddening of the tissue. They appear flushed (reddish), are painful and may be accompanied by a slight edema (figure 2.6.2). The healing process occurs when cells migrate to the epithelial surface. No scars and discoloration is observed after cicatrization;
- **Second degree(II°)** – **partial thickness** – involves the epidermis and a part of dermis. Evidenced in capillary damage resulting in blisters formation. There is a very high concentration of water and albumin in the extra-cellular spaces. In this degree two subtypes of burns can be distinguished:
    - **Superficial dermal (IIa°)** – when the lesion affected the superficial area of dermis (papillary layer). The symptoms are the same of first degree burns with the occurrence of bulky bubbles (figure 2.6.3). These burns heal spontaneously within 7 to 14 days without scaring but with depigmentation;
    - **Deep dermal (IIb°)** – when the lesion is deeper in the dermis. The wound may appear red or whitish (figure 2.6.4) and are little painful. The vascular system is occluded and stagnation in blood flow in the tissue is observed. Healing process is difficult. The recovery is even superior to 15 days after injury and occurs hypertrophic healing. A wound becomes resurfaced from undamaged epithelial cells in the hair follicles and from the margins of the injured area. The new epithelium is thinner when compared to normal. The skin is lighter due to permanent loss of the melanocytes;
- **Third degree (III°)** – full thickness – all epidermal elements and supporting dermal structures are destroyed. The blood flow is stopped. The local nervous system is destroyed. These burns are not painful because the sensory receptors were destroyed. The injury can be white, brownish or black (figure 2.6.4). The spontaneous healing is

impossible and is necessary surgery acts. Resurfacing occurs only from the margin of the healthy skin or by application of a skin graft;

- **Fourth degree (IV°)** – Incineration of tissue from skin to muscle and even bones.

Figure 2.6.2: First degree burns [201].

Figure 2.6.3: Second degree burn – superficial. Figure 2.6.4: Second degree burn – deep [202].

Figure 2.6.5: Third degree burn [202].

The healing process of a wound involves three steps: (1) Inflammatory; (2) Proliferative; (3) Remodeling (figure 2.6.6). Burns that have a high healing potential (HP) are the burns which heals within 3 weeks (healing time). In opposition, the burns with low healing potential are the burns which not heal within 3 weeks. Healing mechanism of wounds is a biologic complex process that involves several intracellular and extracellular mechanisms essentials to the restoration of organism.

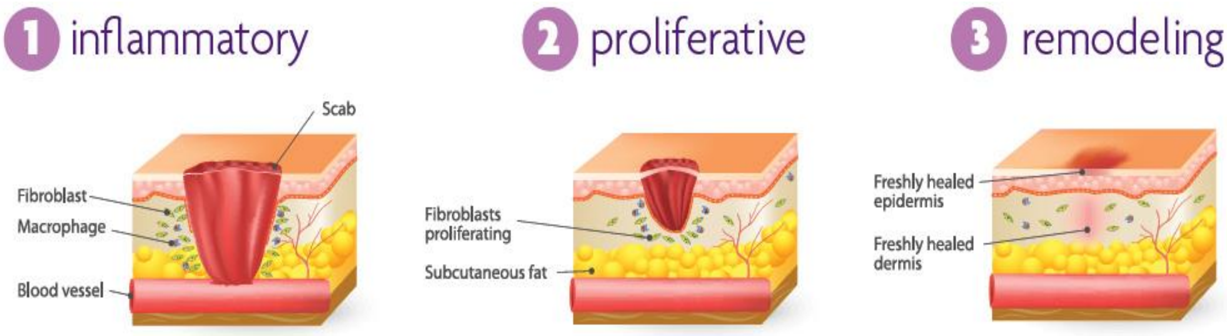


Figure 2.6.6: Steps of wound healing process.

For most burn surgeons, burn depth is better defined by healing potential (HP) based on the time to heal [203]–[205]:

- **Burns that will heal within 3 weeks (high HP)** – generally, superficial wounds that heals by conservative treatment generally by re-epithelialization with minimal scarring;
- **Burns that not heal within 3 weeks (low HP)** – generally, deep burn wound that requires surgical therapy and grafting to prevent a suboptimal result.

Exemplifying, if a partial-thickness burn heals before 2 weeks after the burn injury, scarring is unlikely to occur. On the other hand, after 3 weeks, the risk of hypertrophic scar formation is high. The main limitation of experienced surgeons, in clinical practice, is the differentiation between the IIa° and IIb° wounds because the limit of the conservative or surgical treatment decision is between these wounds degrees [206]. Currently, the errors in the early determination of burn wounds amount are estimated to be 30 %. The results differ according to among individual burn wound treatment clinics and particular performance of physician. The depth limits of both classifications are not well delimited because of the inexistence of a clear division line between the group [207]. Burn depth assessment and healing time is further complicated by the dynamic changes observed in acute post-burn time and can result in the conversion of more superficial to deep burn wound [208]. Sometimes the distinction leads to some errors, such as false positives assessment in that specific cases are undergone to unnecessary surgeries and false negatives with the increase of hospitalization time, contracture, and hypertrophic scar formation.

According to Monstrey *et al.* [207] there were settled down different needs for different specific diagnostics and are divided in three categories:

1- Early assessment of acute burns in the accident and emergency departments where rapid decisions are made concerning the extension and the depth of the burn which determines fluid needs, an eventual referral and the indication for escharatomy;
2- Burn depth assessment for treatment decisions of the actual burn wound to decide if a surgery procedure is required and what to excise or leave;
3- Measurement of burn depth for research purposes: when comparing different treatments, it is essential to ensure that burn depth/severity is similar in each group. This is equally important for research into wound mechanisms to help devise new treatments.

2.6.3. Methods of Burn Assessment

Early assessment of the burn wound depth is extremely important, because of its contribution to the choice of a treatment method. Understanding the relative efficacies of different modalities for evaluating burn depth continues to be a priority.

Clinical Evaluation

The method frequently employed and the least expensive for assessment of burn wound depth is the clinical evaluation. This procedure is based on the subjective external features of the wound such as wound appearance, capillary blanching and refill, capillary staining and burn wound sensibility to light touch and pinprick [209], [210]. These wound features can be readily observed without preparation or specific instrumentation and can be made immediately, easily and without cost [211].

However, this method has 2 significant limitations. The first consists of none of the clinical characteristics for the assessment of burn depth have been 100% reliable and the accuracy is considered to be far from optimal [212], [213]. Although many clinical signs contribute to depth burn determination, only approximately 64% of the time it is done accurately even by experienced burn surgeons [214], [215]. Other study [216] reports that clinical depth assessment is accurate in about 2/3 of cases [214] due the depth overestimation. The second limitation is the validity of diagnosis [211] because there is a variability of burn depth assessments performed by different clinicians [217]. The study made by *Renkielska et al.* [218] reinforces the results of others and showed an accuracy of 62.5% for clinical evaluation.

With this technique the number of accurate prognoses is low with regard to the wound healing time therefore the method should be replaced or supported by another method [219].

Biopsy and Histology

Punch biopsy of burns with subsequent histological analysis is considered one of the gold standard methods for burn depth assessment and constitutes the basis for comparison of other diagnostic modalities [212]. Biopsy provides the patency of dermal vessels and the structural integrity of interstitial and proteins, with occluded vessels and denatured proteins indicative of devitalized tissue [210]. Chvapil *et al*. [220] suggested that microvascular damage is associated to partial-thickness burn, whereas collagen denaturation suggest that is it full-thickness burn. With this method, the assessment of burn is made by staining with hematoxilin and eosin using a thin section of tissue [221]. With the application of staining the assessment determination is performed through the changes between the cellular vitality and the denaturation caused by burns. Even more, for anatomical determination of burn depth the boundary between healthy and necrotic tissue is studied.

Although biopsy and histological analysis is a widely-used method, it has disadvantages. The first is that it is not 100% accurate. When there is no representative portion, sampling errors can occur and tissue shrinkage when a specimen is histologically mounted [210]. In acute time frame, the correlation between structural tissue damage and functional loss may not be accurate, which implies that early biopsies are not wholly accurate, particularly in light of the progressive nature of burns wounds and burn wounds conversion [222]. Another disadvantage is being an invasive procedure, implying additional scarring and consequently an increased risk of developing infections [210]. This modality requires an experienced pathologist and is dependent on the subjective interpretation of the clinician [221]. Biopsy cannot compete in terms of the analysis time with other non-invasive methods currently available. The application of this method for burn depth assessment divides the opinion of several authors. On the one hand, it is stated that despite its limitations, it is an excellent method for confirming the extent of burn that are surgically treated and considered the most accurate method [223]. In the study performed by Renkielska *et al*. [219] the accuracy, sensitivity and specificity of histological assessment was 100%. These results confirm the high diagnostic value. Furthermore, it is suggested that biopsy and histological analysis should not be considered the gold standard for burn depth assessment [207].

There are other modalities based on the measurement of tissue perfusion, since there is a relationship between the depth of burn and microvascular blood flow [224], [225]. The burn wound depth is related to the patency of vessels in the superficial vascular plexus [210]. Due to this relationship, several techniques have been studied to measure the cutaneous circulation or tissue perfusion. These techniques are Vital Dyes, Laser Doppler and Infrared Thermography.

Vital Dyes

The vital dyes are inexpensive but rarely are used for burn depth determination. There are two types of vital dyes: nonfluorescent and fluorescent. The fluorescent involves intravenous injection of fluorescein dye following by ultraviolet light over burned area, which aids in depth visualization, and can detect the dye at specific depth. Due to incomplete penetration of soft tissue, fluorescein fluorescence can neither differentiate between superficial and deep partial thickness burns nor detect viable tissue that is masked by overlying scar [209], [226]. The fluorescein and tetracycline were the earliest fluorescent dyes studied [227], [228]. In case of tetracycline, there were suggested different dosages and injection times and were reported that different depths of skin necrosis were distinguishable to some extent [229]. In case of fluorescein, Bechtold [228], suggested that ultraviolet light was not an absolute necessity for some differentiation of depths.

The most recent dye to be studied is indocyanine green (ICG) and have shown potential value [230]. Using videography with this modality allows the capture of dynamic changes in tissue perfusion [231]. After the injection of indocyanine green, is created a video image of dye uptake and clearance as an indicator of tissue perfusion, through laser fluorescence videography. The normal unburned is used as a control to normalize measurements. When there is an impaired microcirculation, it is associated with a tissue necrosis and the data from ICG angiography can provide dermal viability with high sensitivity [231]. This modality has the advantage of being able to correlate structure with function and being a benign substance that is hepatically cleared [232]. The main limitation is that optical ointments, dressings, and blood interfere with the measurements. Practice standards suggest complete removal of all topical substances from a wound at least 10 minutes before the ICG video angiography to avoid this loss accuracy [233]. Another disadvantage is that the ICG video angiography is expensive and requires sophisticated infrastructure.

Nonfluorescent vital dyes, specifically Evans blue, patient blue V, and bromophenol blue have been studied for use in depth assessment [234] but although can identify surface necrosis from living tissue [229], they are not able to distinguish between partial- and full-thickness burns [209] presenting low clinical utility.

Laser Doppler

Initially, the Laser Doppler was used for monitoring the cutaneous circulation [235]. Doppler principles suggest that when monofrequency lightwaves are reflected off moving objects, they undergo a change in frequency. For instance, laser light directed at moving blood cells in tissue sampled will exhibit a frequency change that is proportional to the amount of perfusion in the tissue [233]. Doppler flowmetry is based on Doppler principles. In the Doppler flowmetry procedure a fiber optic probe is placed directly on the burn wound allowing access to the microcirculation 1mm below the area where the probe contacts the tissue. The accuracy of Laser Doppler flowmetry measure the burn depth ranges from 90% to 97% as compared to 66% with clinical evaluation alone [212], [236]. Also, the positive predictive value is high being approximately 98.4% [237]. Kloppenberg and his team [238] suggested that Doppler Effect not allow for any accurate injury diagnostics and the assessment of the lesion dynamics that occurs within the wound because Doppler Effect cannot differentiate infectious lesions from neoangiogenesis.

Micheels *et al.* [239], [240] have studied the application of Laser Doppler in burns. In their studies, the ability of Laser Doppler to assess microcirculation in burns under varied physiological conditions and its ability to measure the effect of vasodilation was observed. In these studies, there was showed the correlation between the clinical evaluation of depth and the local blood flux of burn. In another study [241], that analyzed 15 patients in the 3 day post-injury, compared the Laser Doppler with clinical evaluation and biopsy and histological analysis. It was concluded that Laser Doppler fully corresponded to histology and was superior to clinical evaluation.

Although flowmetry exhibits high accuracy, this technique has limitations because it requires direct contact with the burned tissue. Since it measures the perfusion in one spot at a time, assessing a large burn wound can be a lengthy and unwieldy process [242].

Laser Doppler imaging (LDI) combines Laser Doppler and scanning techniques and provides a color-coded perfusion map corresponding to different depths of burned area. LDI is the only technique that has been approved by American Federal Drug Administration (FDA) specifically to evaluate the burn wound and has been shown to accurately predict wound outcome with a large weight of evidence. This modality is considered a superior technique comparatively with flowmetry because the whole burn may be sampled and there is no requirement for direct contact with the burn surface avoiding the infection risk and inflict trauma to vulnerable tissue minimizing the patient's discomfort [213]. Recent studies show that LDI suggests reliably predicts the level that distinguishes between burns that will or will not heal by re-epithelialization by 3 weeks [212], [243]. LDI has a very high accuracy, over 97%. Niazi *et al.* [216] reported an accuracy of 100% for LDI assessment comparing to 65% for clinical evaluation. Pape *et al.* [212] reported an accuracy of 97% with the use of LDI. Hoeksema *et al.* [244] reinforced the reliability of these results because it obtained an accuracy of 95% for day 3 post-injury and 97% for day 5 post-injury compared with 52.5% and 71.4% for clinical evaluation. Jeng *et al.* [245] showed that the use of LDI in the estimation of burn depth avoids unnecessary surgery resulting in a reduction of costs and workload and revealed an accuracy of 99% if the wound area is not affected.

The main disadvantage of Laser Doppler Imaging (LDI) and Laser Doppler Perfusion Imaging (LDPI) is that their accuracy is contingent on optics. Because LDI and LDPI are techniques based on optics, heterogeneity and curvature of tissues, topical substances, ambient light, and wound infection can adversely affect depth measurements [246]. Although, the LDI and LDPI are economically expensive modalities, are the latest and most advanced for diagnosing burn wound depth.

2.6.4. Methods of Burn Assessment - Thermography

Although the temperature unit of International System is the Kelvin, in this section will be presented the temperatures values in Celsius degrees, because this unit is commonly used in medical practice on Occidental Europe.

Principles of Thermography in Burns Assessment

There are several techniques available for assessment of burn wound. The previously mentioned methods are either not accurate or difficult to afford. The current medical practice combines the clinical evaluation of wound by surgeon with the biopsy and histological analysis. This combination used is invasive and it is subject to human errors [223]. Thus, there is an urgent need to use a non-invasive method, which would allow the objective and robust classification of the burn wound depth, estimate healing time of burns for treatment planning and assess the treatment progress. This method is the thermography. Thermography is based on the measurement of burn wound temperature.

Infrared thermography is a procedure that detects infrared radiation and produces a temperature pattern of the skin surface.

The blood supply is closely associated with the temperature in this same area of the skin surface. The level of blood supply corresponds to the tissue conditions and reflects its lesions [247]. The burn injuries damage the microcirculation of blood in the wound tissues which is reflected in the change of skin temperature [223] and the temperature pattern of the skin is affected [248]. Thus, the deeper wounds are colder than more superficial ones because of less vascular perfusion near the wound surface [249]. With this correlation, the infrared thermography is able to inversely correlate temperature with depth [249], becoming a well-suited method for the assessment of burn wound depth [211], [223], [250].

Static Thermography

Several authors have discussed the use of thermography to accurately assess the depth of burns. Mladick *et al.* in 1966 verified that thermograms correlated very closely with the pattern of depth of the burns in patients [250].

Some studies [218], [251]–[253] have defined a temperature parameter to classify burn depth. This temperature parameter is ΔT. ΔT corresponds to the difference between the mean values of burned area temperature and the corresponding unaffected area temperature.

In 1974, Hackett [251] performed one of the largest studies in burn patients. In this study, the author compared the mean temperature value of burned area with a similar unburned area. Hackett obtained the following results: if ΔT was -2.5°C or more, a full-thickness burn was diagnosed, in which the burned area had a lower temperature than unburned area; if ΔT value was between -2.5°C and -1.5°C, deep partial thickness burn was diagnosed; if ΔT was less than this, superficial partial thickness burn was diagnosed; if ΔT had a positive value, the burned area had a higher temperature than unburned area and superficial burn was diagnosed; In superficial burns, the perfusion is mainly intact and due to loss of the epidermal layer in these burns, the existing hyperemia is measurable at the surface [254], resulting in a higher temperature than healthy skin and therefore ΔT presented a positive value. In this study, the clinical evaluation failed in 33% of the cases. Thermography was correct in 90% of the cases, therefore this technique was considered to be a superior method of diagnosing the depth of a burn than clinical evaluation.

The authors of study [255] obtained very promising results and demonstrated that the difference between skin temperature in a deeply burn wound was due to the damage in the blood microcirculation and healthy skin can exceed 3.8 ºC.

Watson and Vasilescu [256] reported that full-thickness wound to be more than 2°C cooler than contralateral healthy skin. Still *et al.* [209] presented an accuracy of 90% based on one degree differences in temperature at various aspects of wound.

In a review of Devgan *et al.* [211], it was reported an high accuracy in depth assessment using thermography. However, the obtained results were limited by some aspects such as ambient heat loss [257].

According to Cole *et al.* [258], II°a burns had a ΔT of 1.19 ± 0.97°C, II°b burns presented a ΔT of -1.40 ± 1.17°C and III° burns showed a ΔT of -2.21 ± 1.16°C. Other study of Zhu and Xin [259] reported that for superficial partial skin thickness (II°a), a temperature was in general higher than that of the unburned skin, while in deep partial skin thickness (II°b), it showed a decreased on average by 2.4 °C and concluded that thermography was an effective method of burn depth.

In 2005, Renkielska *et al.*[218], studied the relationship between the ΔT, clinical evaluation and histopathological assessment. In this study, it was reported an accuracy of 62.5%, 89%, and 93.8% for clinical evaluation, histopathological assessment and thermography, respectively. With histopathological analysis, just 6 cases were falsely classified as *non-healing* compared with 22 cases by clinical evaluation. These 6 cases were unnecessarily undergone into surgery. The values of ΔT for II°a, II°b, and III° were of ΔT = 0.96 ± 0.54°C, ΔT = 0.77 ± 0.73°C, and ΔT = -0.44 ± 0.70°C respectively. Furthermore, in this study , Renkielska *et al.* [218], mean ΔT values for surperficial burn of less than 60% dtms (dermis thickness at the measurement site) are positive, while for those deeper than 60% it remains negative. The differences in average temperature between the groups compared were found to be of statistical significance. All the healed burns had a ΔT value positive and in 42 of 43 cases the ΔT values decreased for the burns surficial characteristic range of less than 60% dtms. A total of 71.4% of wounds that did not heal had respective values within the range characteristic for burns deeper than 60% dtms and these were negative. This correlation (ΔT + histopathology) is considerably better than the clinical method (ΔT + clinical evaluation). The ΔT threshold value was defined to be 0.3°C. This value distinguishes the healed and unhealed burns in animal experiments.

The study of Hardwicke *et al.* [252] has intended to verify if infrared thermography can be used along with clinical examination for depth assessment of burn wound. It was concluded that the thermography can correctly determine differences in burn depth. From the study there were obtained the following results: full thickness burns were 2.3 °C cooler that unburned skin area (ΔT=-2.3°C), deep partial thickness burns were 1.2 °C cooler that unburned skin area (ΔT=-1.2°C), while superficial burns were only 0.1 °C cooler (ΔT=-0.1°C). This work also allowed to differentiate superficial and deep burns as shown by Cole [258], [260] and was verified that the increased image and thermal resolution, comparing to LDI (Laser Doppler Imaging) allowed more refinement in classification of superficial partial thickness or unburned area, especially when surrounded by deeper burns. The lowest image resolution of LDI does not match the enhanced detail produced by thermography. Using thermography instead of LDI will allow greater tissue preservation when excising mixed depth burns [252].

Medina-Preciado *et al.* [253] performed a study that compared the value of ΔT obtained by thermography with histopathological measure of burn depth in children. From the 13 burns, 6 were histologically classified as superficial dermal (II°a) and seven as deep dermal burns (II°b). Using thermography, there were obtained the following results: for superficial dermal (II°a), average ΔT of 1.7°C presented increased temperature compared to their contralateral healthy region; for the deep dermal burns (II°b), average ΔT of -2.3°C showed a lower temperature than the contralateral healthy region. Thus, the study demonstrated that there is a significant difference in thermal pattern of deep dermal (II°b) and superficial dermal burns (II°a) and it can be detected through thermography. These thermal differences presented good correlation with histological findings. For a 0°C cutoff ΔT parameter, the thermographic examination agreed with histological results in all of the biopsies while the clinical assessment presented an effectiveness of 61%. The justification for the ΔT negative value for deep dermal burns (II°b) was that it resulted from the blood vessel destruction, which reduced the amount of blood perfusion to the skin and therefore reducing the skin temperature, resulting also in a ΔT positive value for superficial dermal burns (II°a), since this type of burns still have viable tissue, which generated an immunological response that produced inflammation and increased the temperature of the burn wound.

Other study [223] reported that the thermography showed extremely high correlation with the histopathological evaluation of the biopsy material and the clinical examination. The validation of the method was carried out by the comparison with the healing time of a wound. The results demonstrated that the value of ΔT was not statistically significant for superficial burns. However, for deeply burned skin had a temperature lower by more than 3 units of temperature. The experimental results showed that the thresholding value used for the separation between the burns of degrees II°a and II°b is approximately 1.45 ºC below the healthy skin temperature. These results are close to those of Hardwicke *et al* and Medina Preciado *et al*.[252], [253]. With this study, the authors concluded that the thermography allows: the creation of exact isotherm dividing burn area into two parts, superficial and deep, offering to surgeons a new non-invasive tool for aiding in the diagnostic and treatment decision: to operate or not to operate, according to the healing potential of burned patient; also allowed the determination of the correlation between the change of skin temperature and the degree of burn depth (especially II°a and II°b) by comparing the results of biopsy evaluation with the thermographic outcomes.

Burmeister *et al.* [261] performed a study using thermography to analyze if this modality supports the diagnosis of burn severity. In superficial burns undergone in pigs during to 5 -10 seconds, it was verified that at the surface there were warmest, with little change over time. In deep burns undergone in pigs with high contact time (30-40 s), it was verified that wounds became progressively cooler, with a slight decrease in temperature after 1 day after injury. The obtained results confirmed previous reports in claiming that surface temperature decreases with increasing burn depth [252], [253]. The average temperature values in pigs of superficial, deep partial, and full thickness burns obtained were 34.2 °C, 33.4 °C, and 32.6 °C respectively. These outcomes are in agreement with other recent clinical study, which reported an average surface temperature values of 34.5 °C, 33.4 °C, and 32.3 °C for the same measures. Furthermore, this shows that the temperature differences determined are consistent with reports in humans, which found a 2.5°C difference from superficial to full-thickness burns [251]. The results of thermography were significantly correlated with all histological measurements. This study presented data which supports the use of thermography in several ways: improved sensitivity of surface temperature measurements producing consistent differences in surface temperature, determining the burn depth; improved spatial resolution of thermography can highlight specific anatomical areas requiring debridement; improved temporal resolution of thermography allows for visualizing surface temperature measurements in real time; and thermography may be able to predict the extent of ensuing burn progression in the first 4 days. This study also suggested that surface temperature not only predicted the current status of structural damage but is also informative of the spread of necrotic tissue and the zone of stasis.

A recent study, performed by Jaspers *et al.* [254] in 2016, aimed to evaluate the reliability and validity of thermography for assessing the healing potential (HP) of burns. For the validity, they compared the data (ΔT) with the HP results obtained by laser Doppler imaging (LDI), serving as the reference benchmark. The conclusion showed that the thermography had an excellent reliability by the high ICC value of 0.99. For the assessment of validity, it obtained an optimal ΔT cutoff value of -0.07 °C, that allows to differentiate between all burn wounds that are expected to heal and can primarily be treated conservatively (HP <14 days and HP 14 to 21 days), and burn wounds that require surgical treatment (HP >21 days). If the burn wound HP was >21 days, the surgical intervention decision can be made prompt. These results are in agreement with the data obtained by Singer *et al.* [262] who found a cutoff value of 0.1 °C which was rounded to 0°C. Associated with this value, Jaspers *et al.* obtained 80% of sensitivity and 80% of specificity, which has lead to a good validation of burn wounds assessment. However, the authors consider that the validity can be improved and some aspects must be taken into consideration such as: Images obtained by LDI did not correspond to 1:1 with the thermography images due to the thermal camera was sometimes positioned at a slightly different angle or distance; Relatively high number of ΔT values was observed in the distal extremities (hand and feet), and it tend to differ from what is expected based on the LDI results, it was hypothesised that the temperature variation in distal extremities resulted in a ΔT that was influenced by the anatomical location rather than the burn wound [259]. After these results, further research into thermography assessing burn wounds was needed.

In the study of Burke-Smith, Collier and Jones [263] thermography, LDI and Spectrophotometric Intracutaneous Analysis (SIA) were used for burn assessment. The burns were divided according to the time of healing in different groups: Group A to heal within 14 days, Group B to heal in 14 to 21 days and Group C in more than 21 days. With thermography, the group A presented an increase in temperature of 0.89°C (ΔT=0.89°C) comparing to unburned area. In group B the opposite was observed, the temperature of burned area was less 1.80°C than healthy skin (ΔT=1.80°C). Group C presented a decrease of temperature of 1.63°C (ΔT=1.63°C) than healthy skin. In this study, the thermography allowed distinguish between group A and B but not between B and C. LDI was accurate in healing prognosis in only 74% compared to 90% of other literature. The flux of LDI modality revealed a significant difference between group A and B but failed between B and C. LDI overestimated the real group B that instead of to heal within 14 and 21 days, estimated that burns required more than 21 days to heal. This incorrect prognosis led to an unnecessary surgery. The LDI and thermography reported a positive correlation between change in skin temperature of burnt area and mean dermal perfusion. This correlation is consistent because these two modalities only depends on blood perfusion. Results interpretation of SIA were 100% consistent with clinical outcome.

Another study [264], which has used static thermography for evaluate the ability of predicting healing at the 21 days, reported that all superficial partial thickness burns and 11 of 18 deep dermal healed within 21 days. Healed burns were significantly warmer than non-healed burns. Other conclusion was that a cooler burn was associated with longer healing time. So, deeper burns require more time to heal, which is in line with other literature [252], [253], in which deeper burns in histopathological examination and LDI presented cooler temperature.

The study performed by Singer *et al.* [262] in 2015 aimed to evaluate the accuracy of thermography in distinguish the healing of superficial burns that heal in 21 days from those that do not and required surgery. For reference was used the clinical evaluation by an expert surgeon. From the 39-burn wound analyzed, 2 were considered clinically deep and the clinical classification of burn depth was incorrect in another 16 cases. In 15 of these, thermography correctly predicted final burn depth. This study reported an accuracy for thermography of 87.2%, considerably higher than clinical evaluation (54.1%) and it was suggested that thermography could potentially reduce unnecessary surgeries and reduce delays to surgery when necessary.

Dynamic Thermography

The dynamic infrared thermography (DIRT) is the new approach for assess temperature responses following an external stimulation source. There are new methods of stimulation based on active IR thermal imaging, including pulse thermography, phase pulse thermography, halogen lamps, lock-in thermography, with optical excitation but also with ultrasound lock-in thermography. This approach eliminates some of limitations of static thermography on what the influence of external conditions on measurement results is strongly reduced and the classification better defined [205] preserving the positive features. DIRT instead of comparing mean temperature values between burned and unburned skin (static thermography), is based on the difference of tissue thermal properties such as conductivity and thermal diffusivity between burnt and no burnt tissue. After obtaining a baseline reading on the temperature distribution of the area, the tissue is heated or cooled by external stimulation and after the temperature changes are captured [230]. This method provides the answer to one of the most important question: “Will the burn heal spontaneously within 3 weeks of the burn or not?” [219]. This new modality of evaluation of burns seems to be an attractive proposal for quantitative classification, allowing proper choice of burn wound treatment: conservative or surgical, especially compared with static thermography [205].

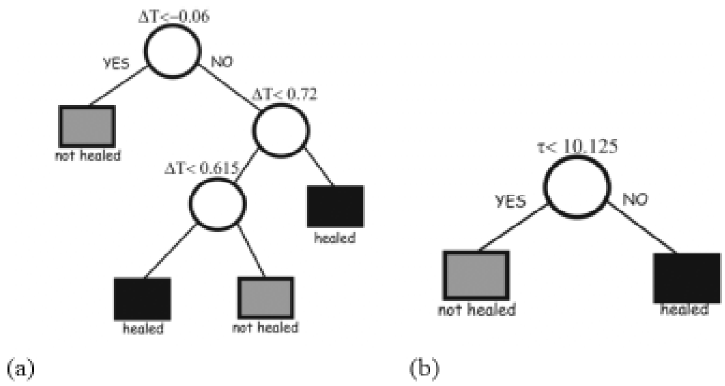
Many authors referred below, that used the dynamic thermography, analyzed the data on basis of a synthetic parameter of DIRT, thermal time constant τ, and the classification of burn wounds is made according to the prediction to heal within 3 weeks, treated conservatively or the prediction to not heal within 3 weeks and surgically treated. For superficial burns—blood perfusion, water content, and heat exchange are increased, which in the dynamic thermography, τ becomes shorter than for unburned skin. Further increase in the depth of burn results in affected blood perfusion and the following rise of the time constant, providing a classification limit. This is equal to the characteristic value of unburned skin. For deep burn wounds—blood perfusion is strongly damaged and heat exchange is decreased. This causes an increase of τ value reaching a longer value. There is a significant probability that the burn will not heal within next 3 weeks [205].

Renkielska *et al.* [219] in 2006 used DIRT with thermal challenge in form of heating by optical irradiation, to analyze burn depth for treatment planning, surgical or conservative treatment. They used animal models, pigs, assessing 32 wounds of different depths and the tissue was histologically assessed to determine the degree of injury. The results obtained from DIRT agreed fully with histopathological evaluations and hence concluded that DIRT is a new effective method for burn wound discrimination and, therefore, for early burn treatment planning.

Another recent study performed in 2014 by Renkielska *et al.* [205] used DIRT with cold excitation for burn depth evaluation and classified the burn wounds according to the healing time: burns that heal within 3 weeks and do not. In the first group were included the burns with depth < 60% of the dermis thickness and from DITI, the obtained value of τ was shorter than the unburned skin. In the second group, the burns were deeper and had a depth bigger than 60%, in which the superficial dermal plexus was totally damaged. For this burn type, the τ was longer than the unburned skin and did not heal in 3 weeks. This study used the histopathological examination as the reference method. The value of thermal time constant for the first group was τ=49.1±23 seconds and for second group was τ=86.3±32.3 seconds. Additionally, was calculated the threshold value and τ=65 seconds was obtained, which generally corresponds to the thermal time constant value of unburned skin. In the animal model with caused wounds, were studied four burn wounds. The number one wound, was obtained a low τ value. The number two and number three, the time constant τ values are close to the unburned skin but still below the threshold value. All these wounds healed totally within 3 weeks. The number four wound had a time constant τ value high and did not heal within 3 weeks. The prognosis performed by DIRT was correctly for all wounds. In other burn wounds presented in this research, the DIRT was efficient because this modality was able to predict the healing time and did it correctly while the clinical evaluation did not. It was also verified the accuracy of DIRT and the histopathological evaluation, which was of 83.9% and 84% respectively. These values are very close but DIRT is non-invasive and requires less time to obtain the results when compared to histopathological evaluation.

Kazmarek et al. [200] aimed to prove if DIRT with external application of pulse may be applicable for burn diagnostics. They proved that this modality can be applied for monitoring the state of the skin and subdermal tissue structure during burns treatment giving objective, measurable ratings of the treatment procedure. It is important to see progress of a treatment especially in a case of complications. DIRT may be used for estimation of burn depth. The initial assumptions applied for DIRT procedures in skin examination were: the skin is a 2- or 3-dimensional medium with at least 3-layer composite structure (epidermis, dermis, subcutaneous tissue); tissue properties are independent on it is initial temperature; external excitation is non-invasive.

Ruminski *et al.* [265] used the DIRT to verify how this modality can determine depth burn. In this study, the static thermography was also applied. Two studies were performed: experimental model and *in vivo* experiments. In the first, with static thermography concluded that temperature of superficial burn was higher than healthy skin and the temperature of deep burn was lower than healthy skin. From the results of transient thermal analysis, it can be concluded that through the time constant (τ) is possible distinguish two groups: deep burns which does not heal in 3 weeks (τ= 9.76 ±0.17 s) and superficial burns which heals in 3 weeks (τ= 11.75 ±0.17). The time constant of healthy skin was also determined (τ= 11.27 ±0.32 s). *In vivo* experiments the results obtained are presented in the figure 2.6.7:



The decision tree generated for (a) the temperature difference ΔT (the static IR thermal imaging figure of merit); (b) the time constant τ in ADT (which automatically determined the threshold value for $\tau = 10.125$ s).

Figure 2.6.7: Results of in vivo experiments performed by Rumin´ski *et al.*. Figure taken from [265].

These results indicate that with DIRT through time constant analysis there was a single threshold value (τ=10.125 s), which divides burn wounds that will heal and those that will not. Thus, with identical results of histopathological examination and time constant analysis, DIRT is considered a valuable clinical tool.

Advantages of Thermography in Burn Assessment

The great advantage of the method is the possibility of assessing large burn areas in an innocuous manner. Furthermore, the growing availability of high quality thermographic cameras and ready-to-use computer software has shown that thermography is a useful complimentary diagnostic tool in medical centers treating burns [207] and the data obtained are mainly used for qualitative assessment [218], [219]. Thermography can support the decision if it is the II ° or the III° degree injury and can provide a clear and objective documentation of burns classification and treatment assessment [200]. This equipment is quick and easy to use [252]. Another advantage of thermography is that can estimate the size of the grafts needed for deep skin burns [204].

Disadvantages of Thermography in Burn Assessment

The thermography also presents limitations. One of inconveniences of the method are the need meticulous care about measurement conditions and the lack of commonly accepted temperature ranges of ΔT for particular burn wound depth classification [219].

The study of Anselmo and Zawacki [266] revealed some drawbacks of this technology due to the evaporative loss of heat or evaporative cooling, which could disguise the temperature differential of a partial-thickness of the wound and lead to a false classification. This incorrect evaluation causes systematics errors interpreting as falsely deep. Furthermore, the accuracy is affected if wounds begin to granulate. However, some techniques that circumvent this such as spraying, drying, and water impermeable membranes, have continued to support the use of IR imaging [267]. Thermography provides optimal results when is done within 3 days of injury [268], [269] because later on the inflammatory processes occurring in the wound tissue change the original temperature distribution in a wound resulting from the blood vessels damage [223].

Concluding, the main advantage of dynamic thermography is the fact that it is a reliable, quantitative diagnostic examination of a burn wound, if is performed as early as the patient is stable, usually at the second day after burn. The thermography modality could potentially determine burn depth and reduce unnecessary surgery as well as reduce delays in surgery if necessary. This non-invasive technique should further improve the diagnostic decision, although more research is needed to fully explore the DIRT outcomes.

Chapter 3

Methodology

This chapter outlines the methodology that will be used throughout this research work. Describing the necessary equipment for image acquisition, the sample characterization, the data collection and analysis protocol as well as the selection of the software and techniques used to obtain the results.

3.1. Ethical Issues

The present study ensures the compliance with the ethical principles for medical research involving human subjects of the World Medical Association Declaration of Helsinki (2013) [270] and is in accordance with the law n °21/2014 that regulates the clinical research in Portugal [271]. The authorization of the ethics committee of *Centro Hospitalar de São João* for the development of research is given in Annex I. The questionnaires presented to the patients during the investigation are in the annexes II and III, respectively for breast reconstruction and for the burn unit.

3.2. Equipment and Software

Data collections were performed using specialized equipment. This equipment ensures the gathering of thermographic images and monitoring of the external variables that can affect the results, such as ambient temperature and relative humidity.

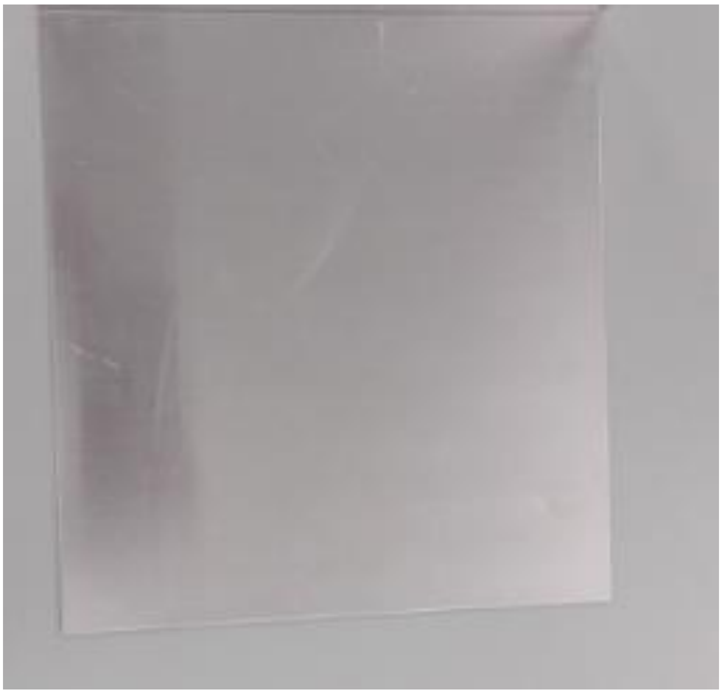
Thermal images were recorded with an infrared camera FLIR E60 sc (FLIR® Systems, Sweden) represented in figure 3.1, whose main features are shown in Table 3.1, and the hygrometer Testo 175 H. For external thermal stimulation used in dynamic thermography with free flap, was used an aluminum plate 22×20 cm that is represented in figure 3.2.

The Testo 175 H is a professional Hygrometer used for monitoring temperature and relative humidity in enclosed places. The use of thermography modality followed the protocol exposed in the Annex IV.

Figure 3.1: Infrared camera E60 sc (FLIR® Systems, Sweden)

Table 3.1 – Characteristics of IRT camera E60 [272].

Spatial Resolution	320 x 240 pixels
Field of view (FOV)	25°x19° / Manual (Minimum focus distance 1.3ft/0.4m)
Minimum distance focus	0.4 m
Image frequency	60 Hz
NEDT	< 0.05°C at +30°C / 50 mK
Measurement repeatability	± 2% of overall reading
Focal Plane Array	Uncooled microbolometer
Focus	Automatic
Measurement analysis correction	Automatic, regions of interest, room temperature and relative humidity



3.2: Aluminum Plate

Regarding software, for this research, it was used the FLIR ThermaCAM Researcher Pro 2.10 software package, which provides tools for data display and analysis and for selection regions of interest and results retrieval [273]. To gather, organize and storage the measurement data, there was used the Microsoft Excel 2013.

3.3. Methods

3.3.1. Study of thermal symmetry of breast in healthy woman

In this research, the section about breast reconstruction in patient with breast cancer, which were in post-operative phase, were assessed with thermal symmetry between two breasts, for benchmarking, it was considered important to study the thermal symmetry in healthy breasts. This study was relevant for obtaining reference values for the four quadrants and nipples of each breast (showed in figure 3.2) since in the literature there are no references in this. For this investigation, eleven women with healthy breasts selected using the criteria of the EURO-QOL EQ-5D questionnaire [274].

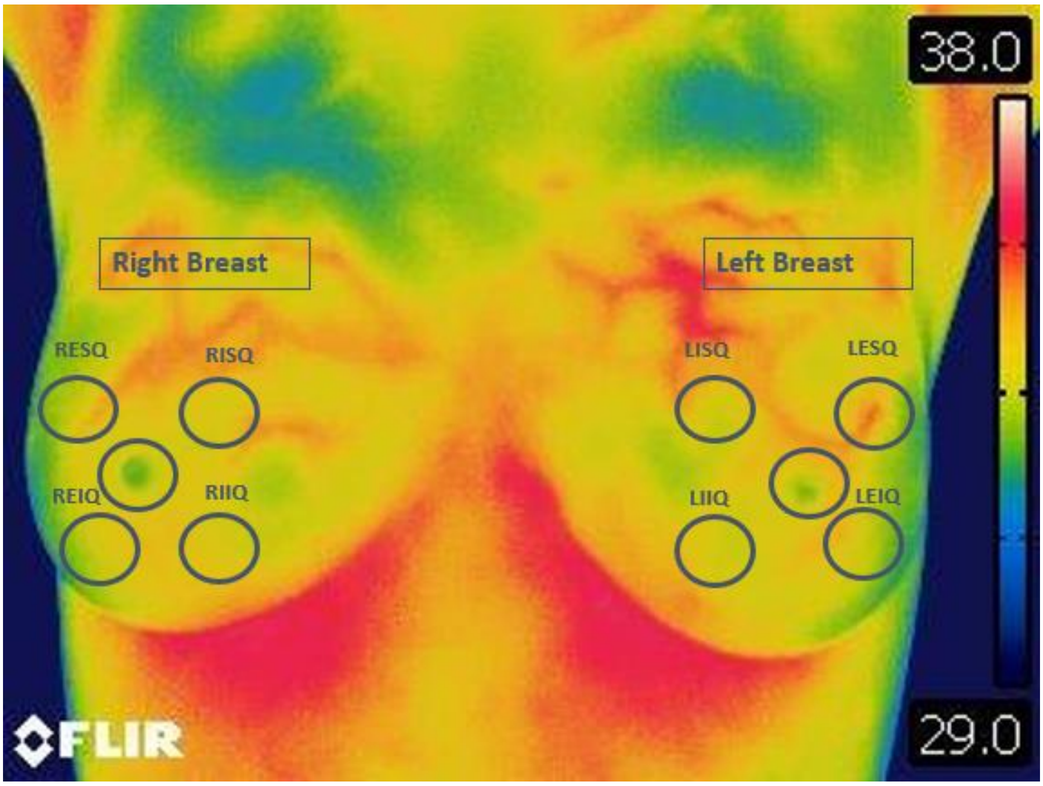


Figure 3.3: Establishment of Regions of Interest (ROIS)

To obtain the thermal symmetry of the breast ΔT, the following calculations were made between quadrants. External Superior Quadrant (ESQ), Internal Superior Quadrant (ISQ), External Inferior Quadrant (EIQ), and Internal Inferior Quadrant(IIQ):

- **ESQ= RESQ-LESQ**
- **ISQ= RISQ-LISQ**
- **EIQ= REIQ-LEIQ**
- **IIQ= RIIQ-LIIQ**

3.3.2. Study of Flaps in Women Submitted to Breast Reconstruction and Other Reconstruction

Static Thermography

Two random participants with age between 27-50 years participated in this study, which was performed at the Centro Hospitalar de São João (CHSJ). Both participants, who done the autologous breast reconstruction, were undergone in mastectomy therapy. In the pre-operative phase, there were collected images of breast and flap area selected for breast reconstruction and analyze the four quadrants of breast. In intra operative phase, there were collected images of flap lifting. In post-operative phase were captured images of reconstructed breast with flap, analyzed the four quadrants and compared the data with pre-operation. In this study, it was also observed the scaring process.

One patient with buttock ulcer participated in study and in this case, there were collected images of the affected area and of the flap area used for reconstruction similarly to the breast reconstruction.

Dynamic Thermography

One random volunteer participated in this experiment, which was performed at the Centro Hospitalar de São João (CHSJ). The participant, who went into autologous breast reconstruction, after mastectomy therapy. Throughout the pre-operative study, the dynamic infrared thermography (DIRT) was applied, through the thermal stimulation during for 1 minute before the images collection. In the studies of Weerd, Weum, and Mercer [188], Weerd, Mercer, and Setså [183] and Weerd, Miland, and Mercer [74] of DIRT application in phases of breast reconstruction the procedure of cool challenge is based on convection methods. In this dissertation will be used a conduction method for thermal stimulation with an disinfected aluminum plate at room temperature, by conduction since it causes a more uniform cooling and avoids the spread of possible microorganisms existing in hospital environment. The images were captured in 0,1,2,3,4,5,6,7,8,9,10 after the stimulation. In pre-operative phase, the flap was marketed with the patient in the specific position according to the donor site, similar to the position of operation, and the thermography examination will be performed. The perforators were earlier marked by surgeon with Doppler method. The main of this study is to verify if the thermography is able to identify the perforating arteries that match the currently impregnated method in plastic and reconstructive surgery service. A graphic was drawn with temperature evolution of two main perforators detected by convectional method and the appearance of hot spots corresponding to the main arteries of the flap was verified. The intra, and post-operative (healing process) were also monitored.

3.3.3. Burns

One random volunteer participated has in this experiment, which was be performed in burned unit at the *Centro Hospitalar de São João (CHSJ)*. The patient was observed and were captured two images: one in the burn site and other in correspondent unburned area. After collections, the images were analyzed, was determined the temperature value of specific zones of burn previously classified by a clinical method, and the ΔT value was calculated, and the result was compared with similar studies. The value of this parameter was used to determine the degree of injury and the result was verified, in which the clinical evaluation has allowed to check whether thermography had presented high accuracy or not for burn depth assessment.

Chapter 4

Results and Discussion

This chapter will present the results of this research, its main conclusions, and discussion. First, the study of thermography in women with healthy breast will be demonstrated and then each case of study of plastic and reconstructive surgery and their discussion.

Thermal Symmetry in Healthy Breasts

The thermal symmetry analysis of healthy breasts is exposed in table 4.1. The thermal symmetry was calculated for nipple and for four quadrants of breasts: External Superior Quadrant (ESQ), Internal Superior Quadrant (ISQ), External Inferior Quadrant (EIQ), and Internal Inferior Quadrant(IIQ). In table are presented the mean ΔT value and standard deviation of sample. It can be verified that at the maximum this value was of 0.74±0.51°C at the studied ROIs.

Table 4.1: Thermal symmetry analysis

ROI's	MEAN ΔT	Standard deviation
ESQ	0.74	0.51
ISQ	0.71	0.43
EIQ	0.48	0.32
IIQ	0.5	0.31
Nipple	0.37	0.30

As one of the purposes of this dissertation is the monitoring of the autologous breast reconstruction, was considered relevant, to study the temperature values of the four breast quadrants and nipples in healthy women in order to obtain an indication of reference values to assess the thermal symmetry in the postoperative period because it is considered an important aspect. The study was performed in eleven healthy women and through the analysis of table 4.1 was verified that the ΔT value for each ROI was less than 1°C. The highest temperature difference in healthy breasts was recorded for the ESQ quadrant, but not significant being very close to the remaining quadrants. The nipples, a sensitive area of breast, presented a slight difference between two breasts, revealing a high thermal symmetry. The standard deviation for all regions of breast was less than 1 revealing reduced variability of sample values. This analysis was important since it was never done and still constitutes an indicator of thermal symmetry of healthy breasts.

Cases of Study

4.1. Case of Study 1

4.1.1. Description of case

The first case study is related to a male with 41 years and BMI of 27.55 kg/m^2. This patient is paraplegic from the age 10-12 years with an unknown etiology. The patients presented a sciatic ulcer in right side. He was hospitalized in the plastic and reconstructive surgery service to remove the ulcer and to reconstruct with autologous tissue using the major gluteal flap. The digital image of ulcer is shown in figure 4.1.1.

Figure 4.1.1: Image of affected zone (ulcer) at pre-operative phase.

4.1.2. Flap Selection

Due to the ulcer is located in low zone of gluteal, the selected flap was the major gluteal flap. The image 4.1.2 is exposed the area of flap that was used in reconstruction.

Figure 4.1.2: Image of selected flap.

4.1.3. Aim, Methods, and Collection Conditions

For this study there were collected images in pre, intra and post-operative phase in order to compare the temperature values of respective regions of interests (ROI's) in different phases of intervention. In this case, it was applied the methodology of static thermography described in detail in section 3.3.2. The chosen ROI's is the flap area demonstrated in figure 4.1.3. and were selected several points in border flap in post-operative time for monitoring healing process. The collection environmental conditions are exposed in table 4.1.

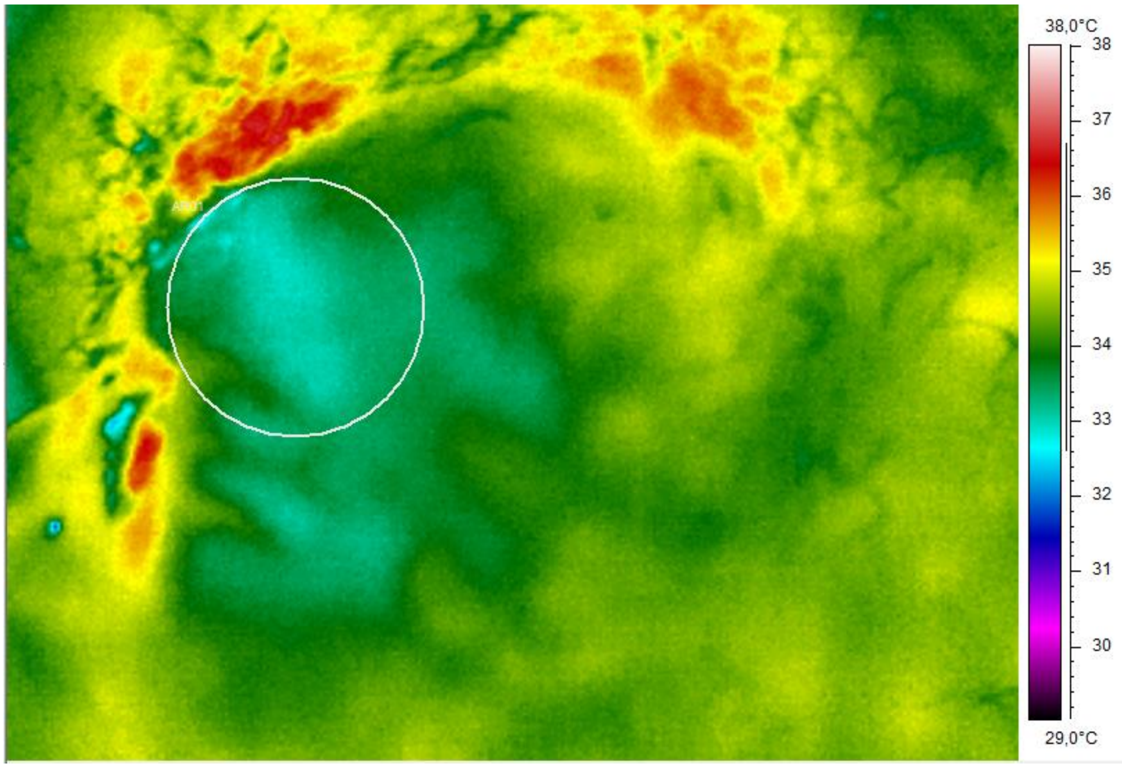


Figure 4.1.3: Thermal image of ROI.

Table 4.2 - Collection environmental conditions

PHASE COLLECTION	COLLECTION TIME	TEMPERATURE (°C)	RELATIVE HUMIDITY (%)
PRE-OPERATIVE	Previous day of surgery	22.2	51.6
INTRA-OPERATIVE	Day of surgery	20.9	59
POST-OPERATIVE	7 days after surgery	22.7	54

4.1.4. Results of pre-operative phase

At this stage, there was collected an image of affected area to register the total area submitted to the surgery and the selected flap. The corresponding thermal image is presented in the next figure.

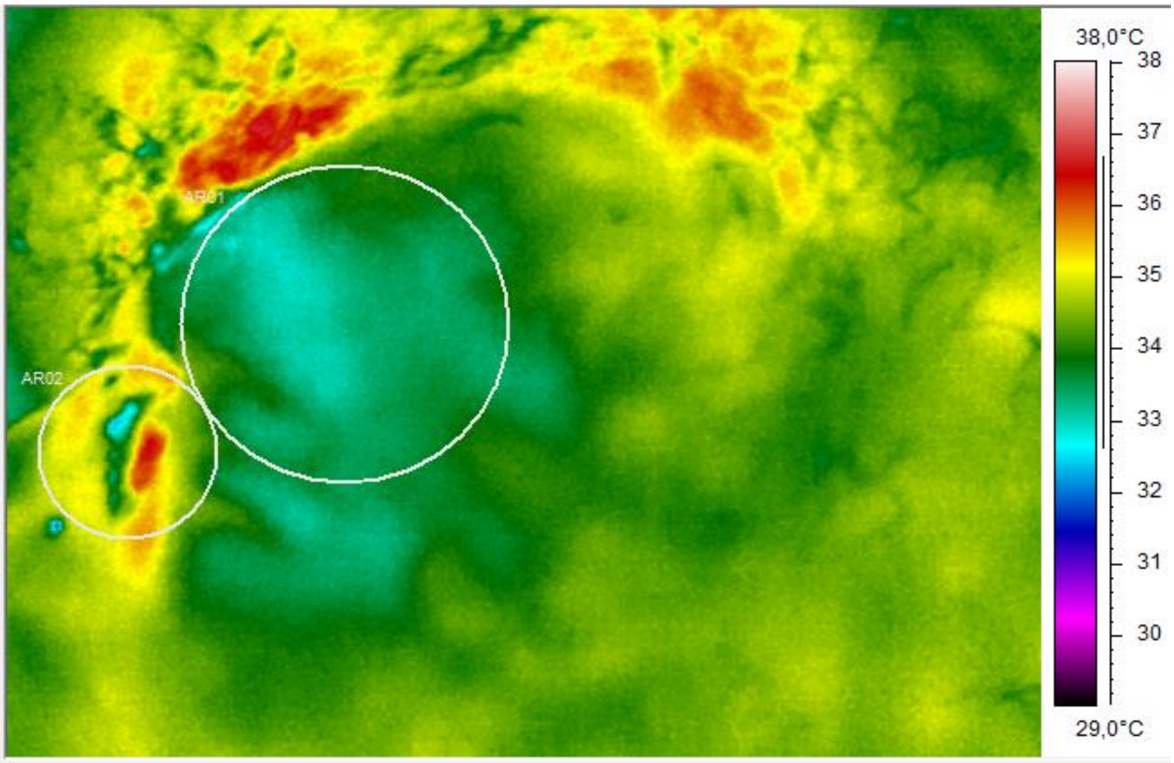


Figure 4.1.4: Thermal image captured in pre-operative phase of affected zone submitted to the reconstruction and the selected flap.

The analysis of ROI's, the gluteal flap and the ulcer are presented in table 4.3.

Table 4.3 - Analysis of ROI's of pre-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	33.5	34.7
ULCER (AR02)	34.8	36.6

The results of mean temperature value of flap and ulcer are close but the mean temperature value was higher for ulcer.

4.1.5. Results of intra-operative phase

At this stage, there was captured an image during the surgery in time of flap lifting before the reconstruction has been completed, before closing the ulcer. The digital photography is exposed in image 4.1.5. and its thermal image is presented in figure 4.1.6.

Figure 4.1.5: Digital image of flap selected (gluteal flap) at intra-operative phase.

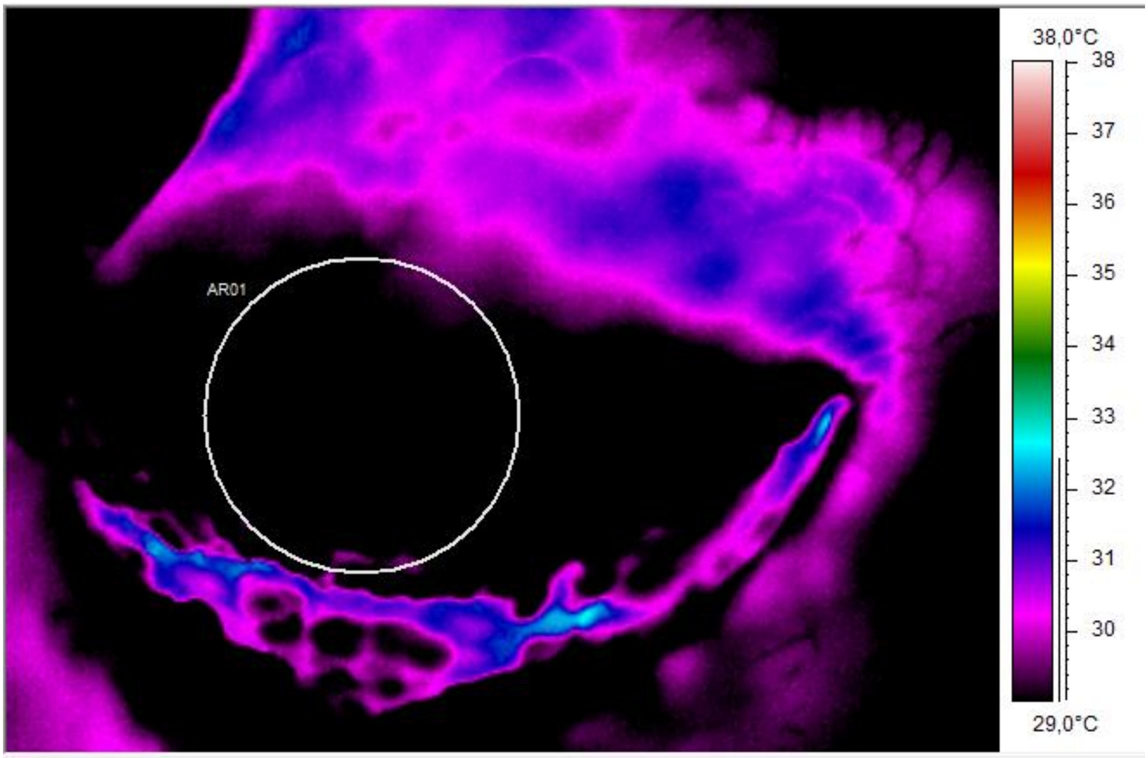


Figure 4.1.6: Thermal image of flap selected (gluteal flap) at intra-operative phase.

The analysis of corresponding ROI is presented in table 4.4.

Table 4.4 - Analysis of ROI (flap) of intra-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	27.5	29.8

Through analysis of data exposed in previous table, it is possible to observe low temperatures values on the flap, when comparing them to the values obtained in the pre-operative period.

4.1.6. Results of post-operative phase

The collection of images for the post-operative moment was done at 7 days after reconstructive surgery. At this stage, the temperature values of superficial skin of reconstructed area and the healing process through were assessed through analysis of temperature values of located points on the flap edge where it was sutured. The digital image of flap after intervention is presented in figure 4.1.7 and its thermogram is exposed in image 4.1.8.

Figure 4.1.7: Digital image of flap (gluteal flap) at post-operative phase.

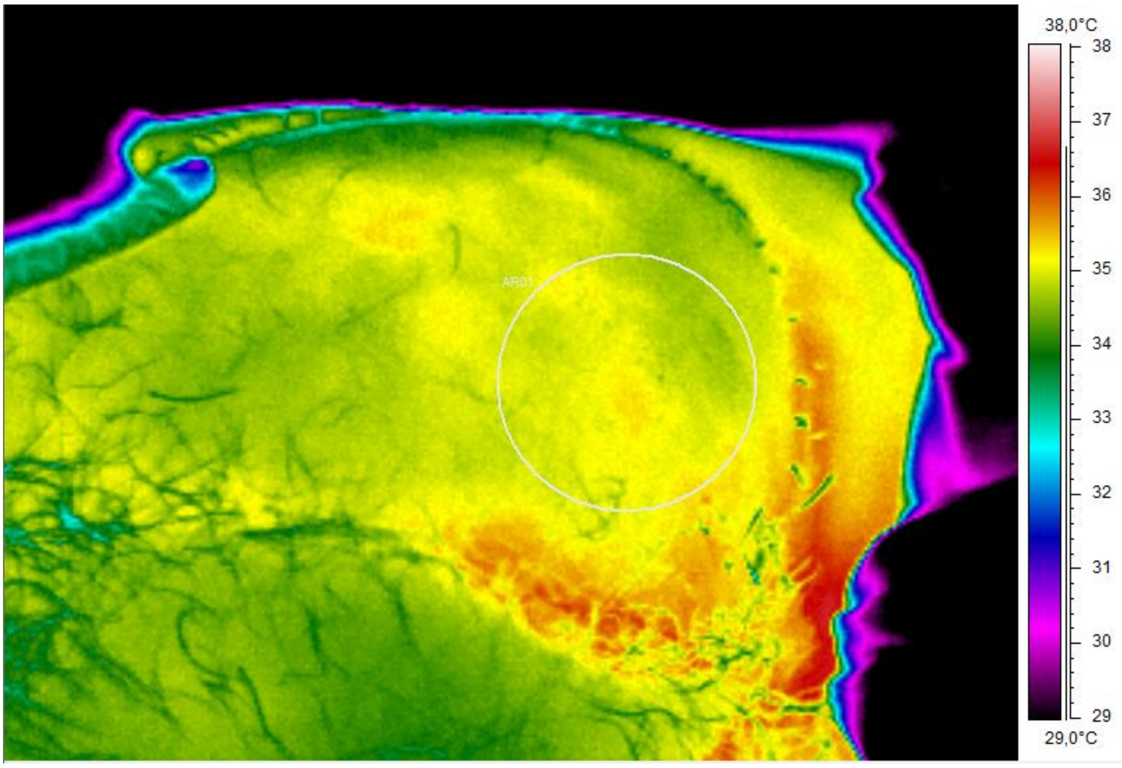


Figure 4.1.8: Thermal image of flap (gluteal flap) at post-operative phase.

The analysis of ROI is presented in table 4.5.

Table 4.5 - Analysis of ROI (flap) of post-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	35	35.5

As previously mentioned, one of the purposes of this research is to study the healing process of autologous reconstruction. For this, it was established several ROI's located in the suture zone of the flap as shown in thermal figure 4.1.9.

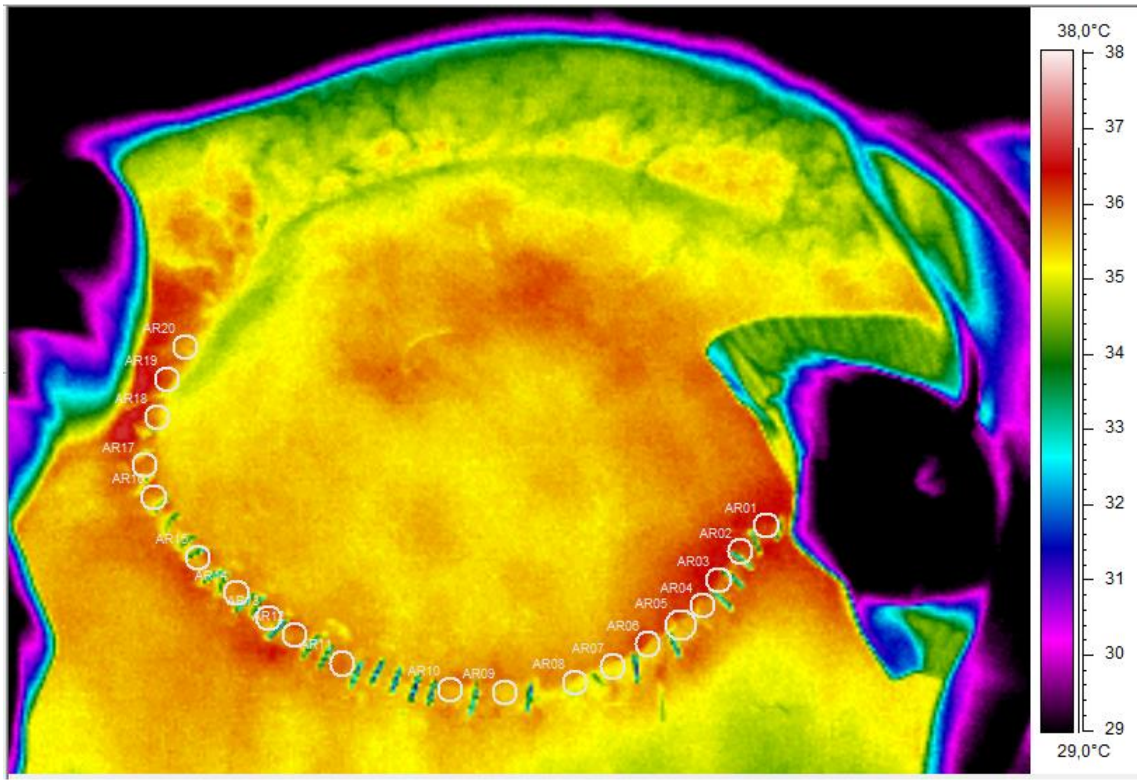


Figure 4.1.9: Thermal image of flap (gluteal flap) and ROI's at post-operative phase.

The analysis of selected ROI's for healing process study is presented in table 4.6

Table 4.6 - Analysis of ROI's of healing process of post-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
AR01	36	36.5
AR02	35.7	36.4
AR03	35.7	36.5
AR04	35.8	36.3
AR05	35.6	36.3
AR06	35.7	36.3
AR07	35.4	36
AR08	35.3	35.8
AR09	35.5	35.9
AR10	35.7	36
AR11	35.8	36
AR12	35.9	36.2
AR13	35.4	36.2
AR14	35.4	36
AR15	35.4	36.2
AR16	35.5	36.1
AR17	35.7	36.1
AR18	35.6	36.2
AR19	35.9	36.6
AR20	35.7	36
MEAN	**36**	**36**

4.1.7. Discussion of Study Case 1

Having in consideration the results exposed in this case of study, in pre-operative phase the flap shown a mean temperature value of 33.5 °C and the affected zone, sciatic ulcer, presented a mean of temperature value of 34.8 °C. The difference of the temperature values is 1.3°C, being superior at the ulcer zone. The higher temperature value for ulcer zone can be justified by the consequences associated to the ulcer, such as the inherent bleeding and possible inflammation process. These two factors are sufficient to raise the temperature in affected zone relatively to the flap.

The thermal images at the intra-operative phase of lifting demonstrated temperature values lower than the pre-operative phase. The corresponding ROI to the flap showed a mean temperature value of 27.5 °C. The difference of mean temperature value of the flap between pre and intraoperative phases was of 6°C. This value is very high and demonstrates a significant different between the two phases. This difference cannot be real because during the surgery procedure the patient body is covered by iodopovidone, a substance used as disinfectant and before the image been captured, the nurse cleaned the blood surrounding the flap area. So, these fluids can affect the original thermal pattern of the surface of the skin translating that into the results obtained, which cannot be used for any type of analysis. The temperature values observed at the operating room were very lower when compared with the infirmary, where the pre-operative images and post-operative images were taken. These aspects are sufficient to justify this discrepancy between the flap temperature values at different phases.

The results of post-operative phase presented a mean temperature value for the flap of 35°C. The difference of temperature values between pre and post-operative was 1.5 °C. The increase of temperature value in post-operative phase is justified by the healing process associated. The selected ROI (gluteus) is close of suture zone where are unleashed different steps of healing process that are: inflammation, proliferation and differentiation. These mechanisms are associated to a high metabolism, representing the high temperature values. The ROI's associated to the healing process located in suture zone presents temperature values (36°C) higher than the results of flap in all phases of surgery process. These closer differences suggest that there is an associated healing process, but not with an infection process, which would be the case of having higher differences. The fact of these points has a higher temperature suggests that the healing process is progressing as expected and does not demonstrates principles of tissue necrosis, which could be characterized by a decrease of temperature in intervened area.

The surface temperature of the flap suggests a good clinical evolution, which was confirmed, 1 month after surgery, by clinical evolution and by no complications associated with this subject.

4.2. Case of Study 2

4.2.1. Description of case

The second case of study corresponds to a woman with 46 years and BMI equals to 26.35 kg/m^2. This patient in 2005 had breast cancer on the right side and at that time underwent lumpectomy, in which the tumor was removed, and radiation therapy. In 2009 had left breast cancer and underwent mastectomy and immediate breast reconstruction with TRAM and posterior chemotherapy (4 cycles). This woman was admitted to the hospital to complete the right mastectomy and immediate reconstruction with pedicled *Latissimus dorsi* flap. In figure 4.2.1, 4.2.2 and 4.2.3. are exposed the breasts of patient before the surgery.

Figure 4.2.1: Digital image of breasts in pre-operative phase.

Figure 4.2.2: Lateral digital image of right breast in pre-operative phase.

Figure 4.2.3: Lateral digital image of left breast in pre-operative phase.

4.2.2. Flap Selection

This patient was submitted to another breast reconstruction in 2009 using TRAM flap for left breast and so in this surgery was chosen the *Latissimus dorsi* muscle. In next figure 4.2.4 is exposed the image of selected flap for breast reconstruction. The pedicled flap used constitutes advantages: simplifies surgery and decreases its duration as mentioned in literature review.

Figure 4.2.4: Digital image of *Latissimus dorsi* flap in pre-operative phase.

4.2.3. Aim, Methods, and Collection Conditions

In this case of study, the data collections were obtained in pre, intra and post-operative phases. The methodology applied was the static thermography described in section 3.3.2. and its analysis was performed in order to compare the temperature values of respective regions of interests (ROI's) between pre, and post-operative phases. The ROI's selected for analysis was four breast quadrants around the nipple and the nipple: RESQ, RISQ, REIQ, RIIQ, RN (right nipple), LESQ, LISQ, LEIQ, LIIQ and LN (left nipple) (figure 4.2.5). These quadrants are shown in the figure below. The bilateral thermal symmetry in post-operative phase will be studied with calculation of ΔT right breast and left breast for four selected quadrants around the nipple. As previously mentioned, one of the purposes of this research is to study the healing process of autologous breast reconstruction. For this study case, this task was difficult because in moment of data collections of post-operative phase the patient contained medical dressings. The conditions of environmental conditions for all collections are exposed in table 4.7.

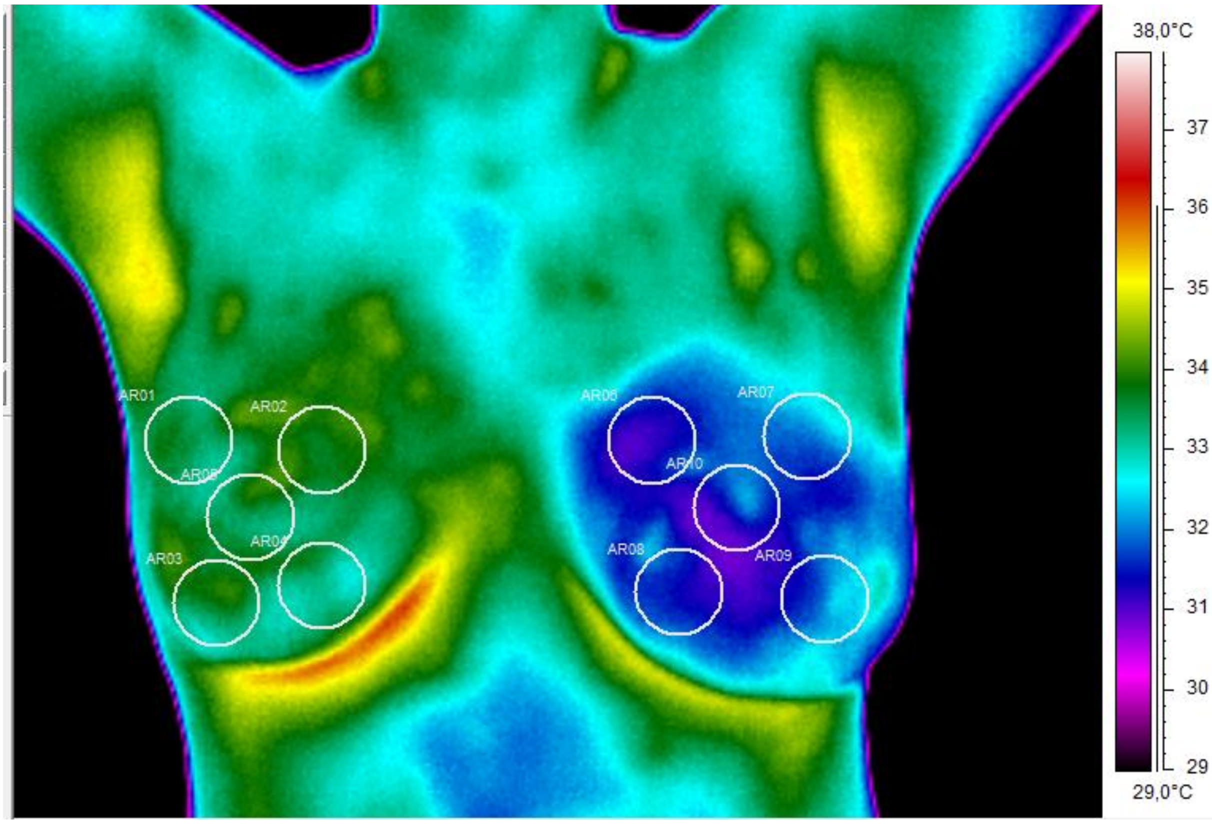


Figure 4.2.5: ROI's selected.

Table 4.7 - Collection environmental conditions

PHASE COLLECTION	COLLECTION TIME	TEMPERATURE (°C)	RELATIVE HUMIDITY (%)
PRE-OPERATIVE	Previous day of surgery	21.7	52.9
INTRA-OPERATIVE	Day of surgery	21	64.4
POST-OPERATIVE	4 days after surgery	22.1	53.8

4.2.4. Results of pre-operative phase

At pre-operatory phase, there were collected thermal images of breast before the surgery to register the area submitted to the surgery and the selected flap for reconstruction to obtain their characteristic temperature values. These thermal images are presented in the next figures 4.2.6 and 4.2.7 and temperature values exposed in tables 4.8 and 4.9 respectively.

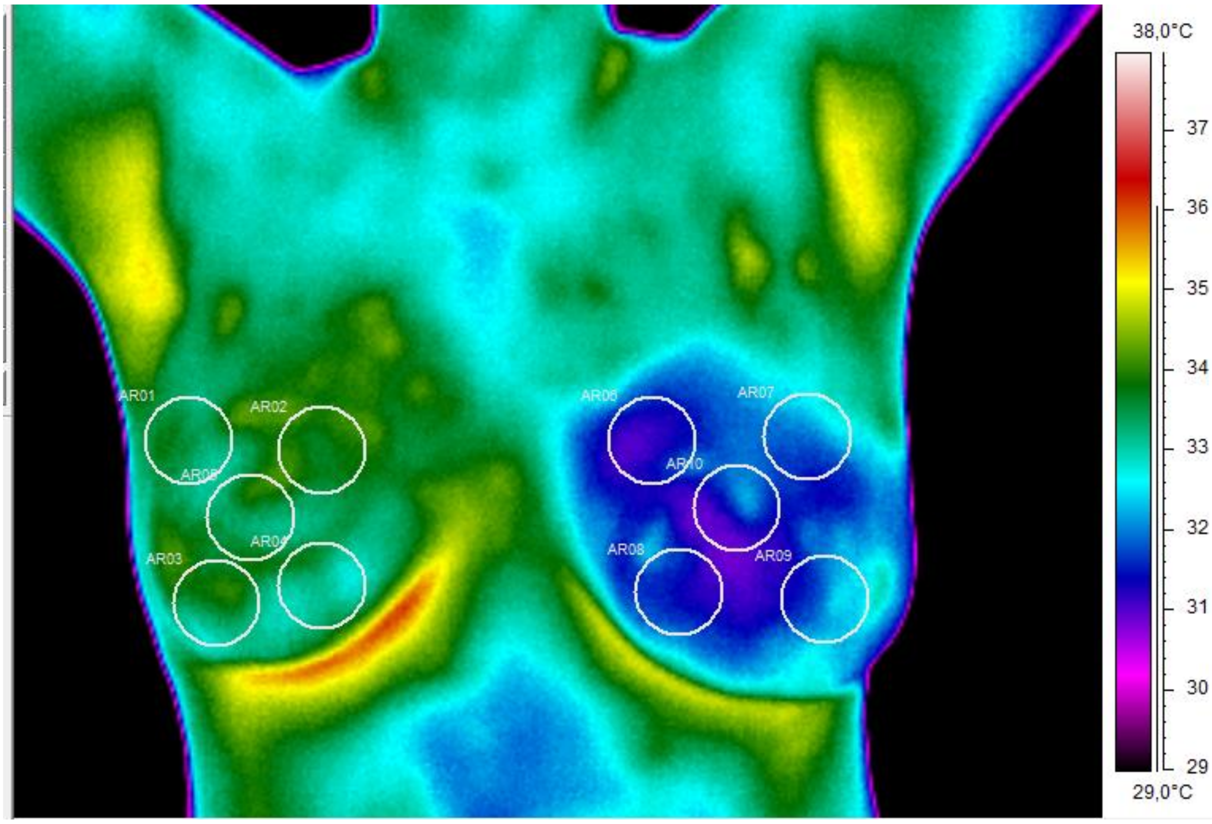


Figure 4.2.6: Thermal image of four of breast quadrants and nipple.

Table 4.8 - Analysis of ROI's of pre-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
RESQ (AR01)	33.5	34
RISQ (AR02)	33.9	34.3
REIQ (AR03)	33.6	34.2
RIIQ (AR04)	33.3	33.8
NR(AR05)	33.5	34.2
LISQ (AR06)	31.4	32.1
LESQ (AR07)	32.2	33.2
LIIQ (AR08)	31.6	32.4
LEIQ (AR09)	32.2	33.1
NL(AR10)	31.5	32.3

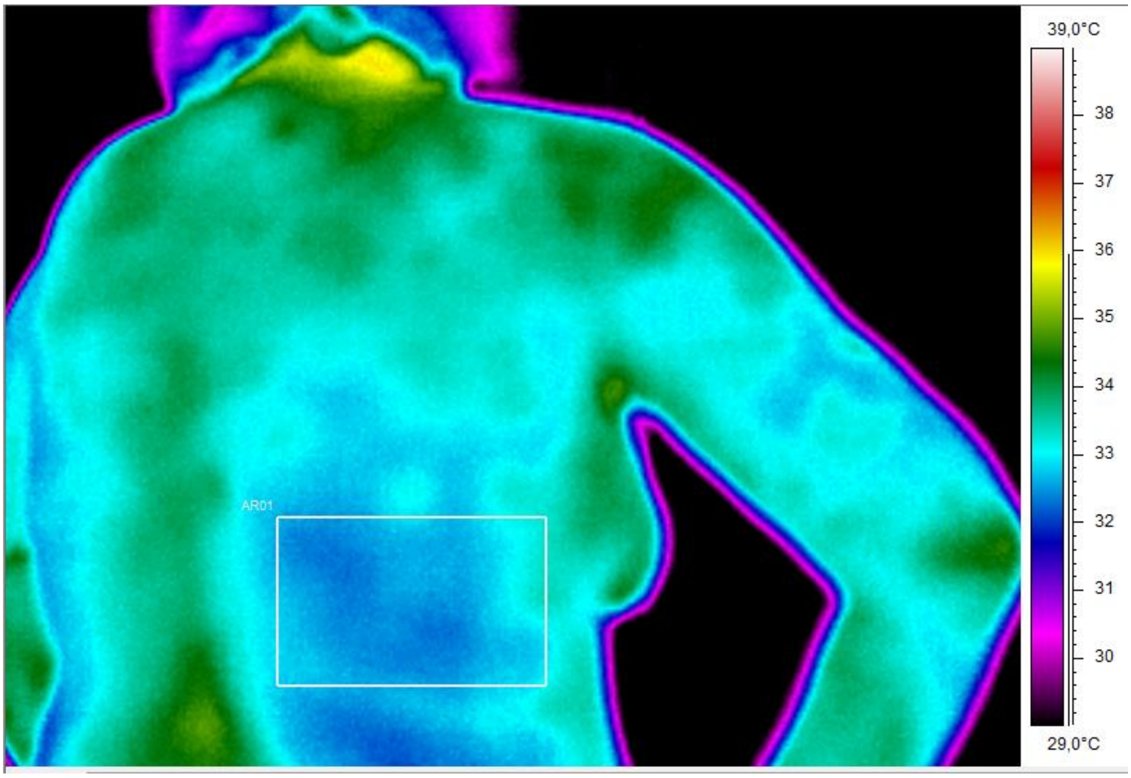


Figure 4.2.7: Thermal image of flap selected, *Latissimus dorsi* muscle.

Table 4.9 - Analysis of ROI of pre-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	32.7	33.5

4.2.5. Results of intra-operative phase

At surgery, there were captured images of flap lifting before the reconstruction has been completed. The digital photography is exposed in image 4.2.8 and its thermal image is presented in figure 4.2.9.

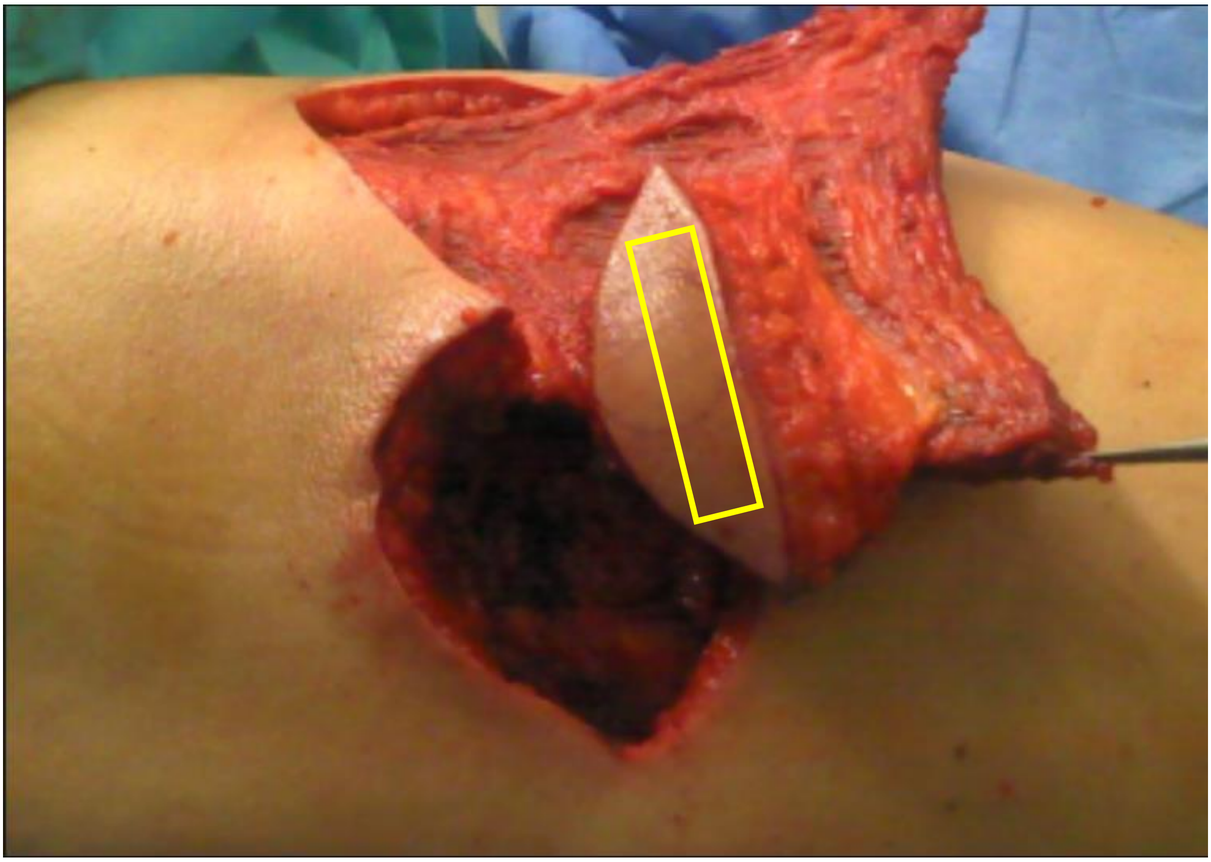


Figure 4.2.8: Digital image of flap selected *Latissimus dorsi* muscle at intra-operative phase.

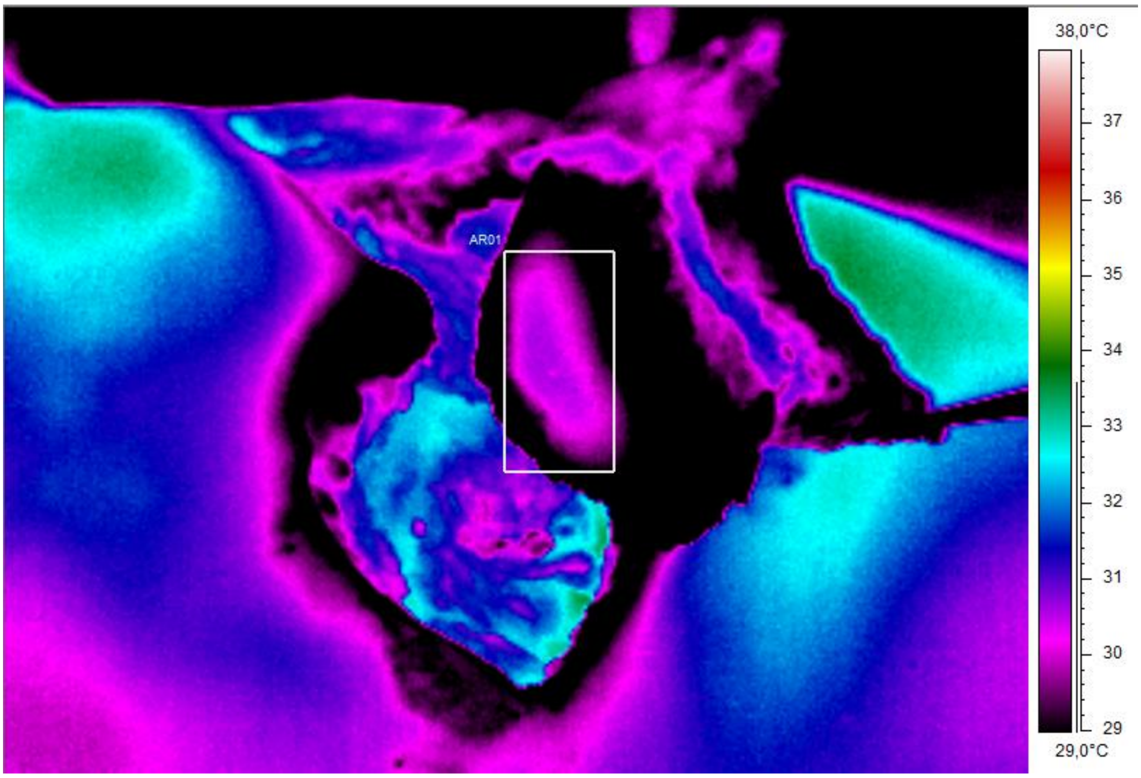


Figure 4.2.9: Thermal image of flap selected, *Latissimus dorsi* muscle at intra-operative phase.

The data obtained of the ROI is presented in table 4.10.

Table 4.10 - Analysis of ROI (flap) at intra-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	29.6	31.4

Through the analysis of the data exposed in previous tables, it is possible to observe lower temperatures values of flap when comparing to the values obtained at the pre-operative period.

4.2.6. Results of post-operative phase

The post-operative monitoring was done at 4 days after breast reconstruction. The digital image of flap after intervention is presented in figure 4.2.10 and its thermogram is exposed in image 4.2.11.

Figure 4.2.10: Digital image of breasts after surgery. a) Right breast submitted to autologous reconstruction and left breast; b) Right reconstructed breast.

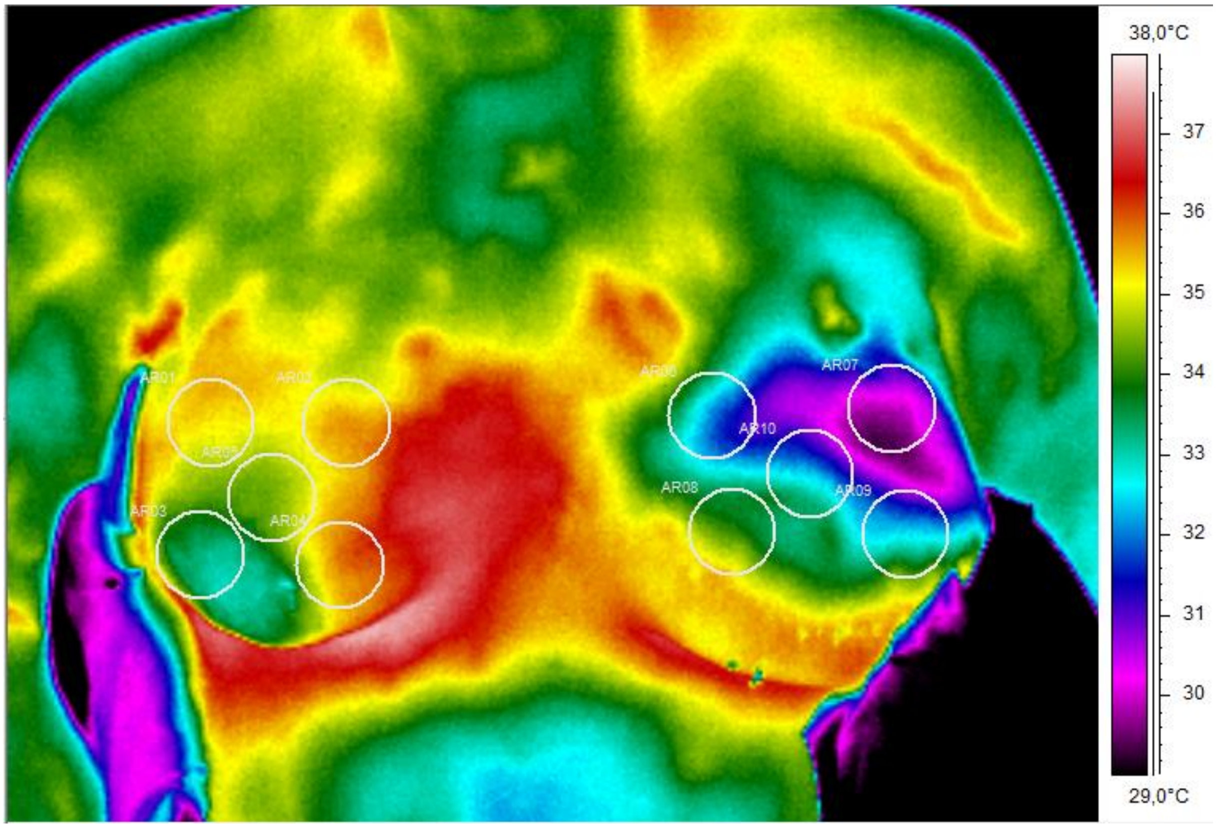


Figure 4.2.11: Thermal image of four breast quadrants in post-operative phase.

The data obtained of ROI's, breast quadrants, are presented in table 4.11 and the differences of temperature of different quadrants are presented in table 4.12.

Table 4.11 - Analysis of ROI's of post-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
RESQ (AR01)	34.8	35.5
RISQ (AR02)	35.1	35.6
REIQ (AR03)	34.1	35.6
RIIQ (AR04)	35	35.8
NR(AR05)	34.5	35.3
LISQ (AR06)	32.6	33.5
LESQ (AR07)	30.2	31.7
LIIQ (AR08)	35.1	35.4
LEIQ (AR09)	34.6	35.7
NL(AR10)	32.2	33.8

Table 4.12 - Differences of temperature between quadrants of breasts

Breast Quadrants	ΔT value (T right breast- T left breast)
ESQ	4.6
ISQ	2.5
EIQ	-0.5
IIQ	-0.1
Nipple	2.3

4.2.7. Discussion of study case 2

According to the results obtained at pre-operative phase, the four quadrants presented different mean temperature values between two breasts. In right breast, submitted in to mastectomy and immediate reconstruction presented similar temperature values for all quadrants and the interval of mean temperatures was [33.3-33.9]˚C. In left breast presented interval of temperature values for quadrants of [31.4-32.2]˚C. In this breast, the intern quadrants presented lower mean temperature value comparing to external quadrants. In case of left breast, the general temperatures of all quadrants were lower than the right breast and this fact may be due to the mastectomy performed in 2009 with autologous reconstruction through TRAM flap and so the tissue does not contain the natural characteristics of breast tissue such as your original blood network. The flap obtained a mean temperature value of 32.7 ˚C that is close to the temperature values of breasts.

Like the thermal images collected, in intra-operative phase of study case 1, the flap presents a lower mean temperature, 29.6 ˚C that can be explained by the application of *iodopovidone* substance in body of patient during the surgical intervention. So, it is not possible to make any conclusions about the thermal pattern of the flap in intra-operative phase.

The data of post-operative phase revealed an increase of mean temperature values for all quadrants of two breasts, except for left breast external superior quadrant (LESQ). The temperature interval for right breast is [34.1-35.1]˚C and for left breast is [30.2-35.1]˚C. This general increase of temperature for two breasts can be associated to healing process associated because both breast were intervened, the right for mastectomy and immediate reconstruction and the left for balance in terms of esthetics with right breast. The quadrant that had lower temperature value (LESQ) does not corresponds to the suturing area, however, it does not suggest a possible necrosis situation to justify this significant decrease of mean temperature value.

In post-operative phase, it was considered important to determine the bilateral symmetry of breasts calculating the ΔT value between the same quadrant. These values are presented in table 4.12 and demonstrates that only for EIQ and IIQ quadrants present an excellent thermal symmetry (< -0.5ºC), revealing that for left breast the temperature was higher. For other quadrants, there are significant discrepancies that may be due to the fact that there are some differences between the breasts such as the lack of nipple in the left breast, the suturing zones are different, and still due to the fact that the suturing zones still have medical supplies.

After the collections, it was known that this patient has a good clinical prognosis without flap loss.

4.3. Case of Study 3

4.3.1. Description of case

The patient studied in case 3 is a woman, with 27 years, with BMI of 23.03 kg/m^2. This patient was diagnosed with breast cancer in left side in December of 2014. In this time was undergone to the neo-adjuvant chemotherapy with ovarian suppression, radiotherapy and hormone therapy. In June of 2015 she was submitted to radical mastectomy and at this date the breast reconstruction was not performed. At this experiment, the patient was admitted to Hospital in order to reconstruct the mastectomized breast. The state of breasts is present in the figures 4.3.1 to 4.3.3.

Figure 4.3.1: Digital image of breasts at pre-operative phase.

Figure 4.3.2: Lateral digital image of right breast at pre-operative phase.

Figure 4.3.3: Lateral digital image of left breast (mastectomized) at pre-operative phase.

4.3.2. Flap Selection

In the figure 4.3.4, it is exposed the digital image of flap used for breast reconstruction. The flap chosen for this intervention was the *Latissimus dorsi* muscle.

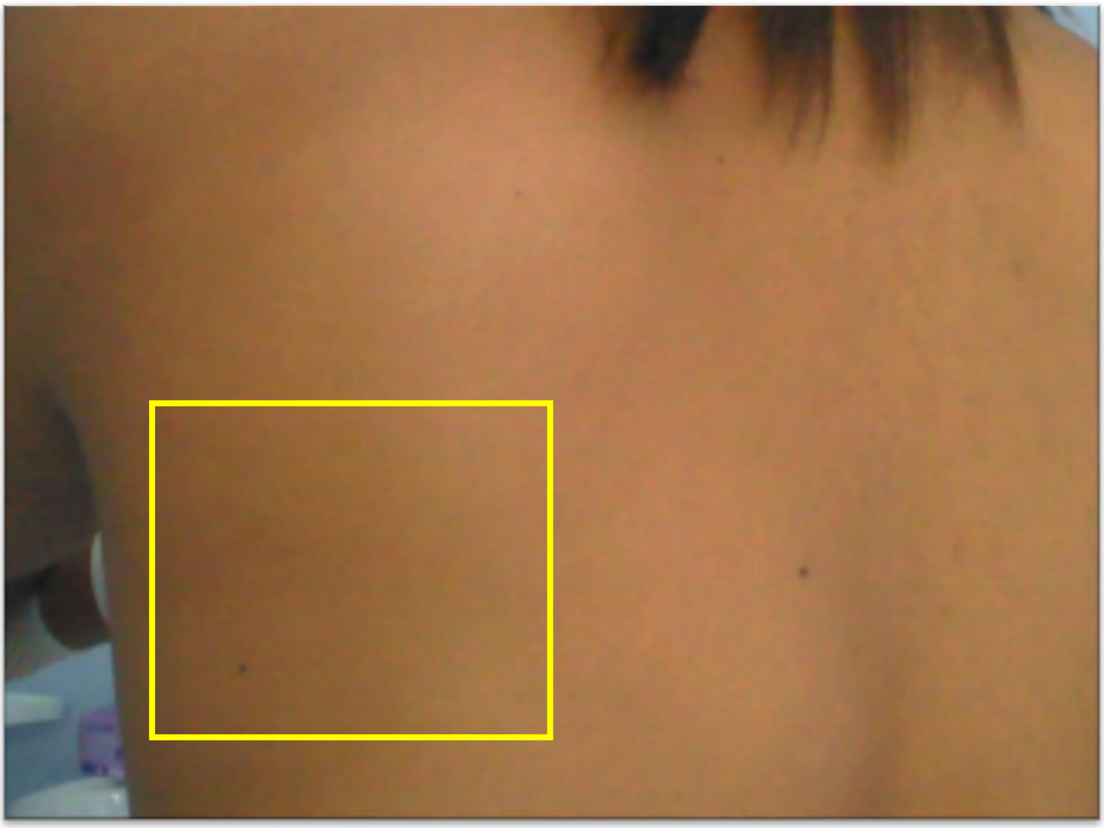


Figure 4.3.4: Digital image of *Latissimus dorsi* flap at pre-operative phase.

4.3.3. Aim, Methods, and Collection Conditions

The static analysis was performed in order to compare the temperature values of respective ROI's between pre, and post-operative phases. The ROI's selected for analysis to compare the data were four breast quadrants around the nipple and the nipple: RESQ, RISQ, REIQ, RIIQ, RN, LESQ, LISQ, LEIQ, LIIQ and LN. These ROI's are shown in the figure below (4.3.5), it is important to note that the ROI's at the left breast had an approximate location since there was no breast present as a result of mastectomy. The bilateral thermal symmetry in post-operative phase will be studied with calculation of ΔT for all quadrants.

In this case of study, the images (digital and thermal) were collected at pre, intra and post-operative phases. The methodology was the static thermography previously described. The collection environmental conditions are exposed in table 4.13.

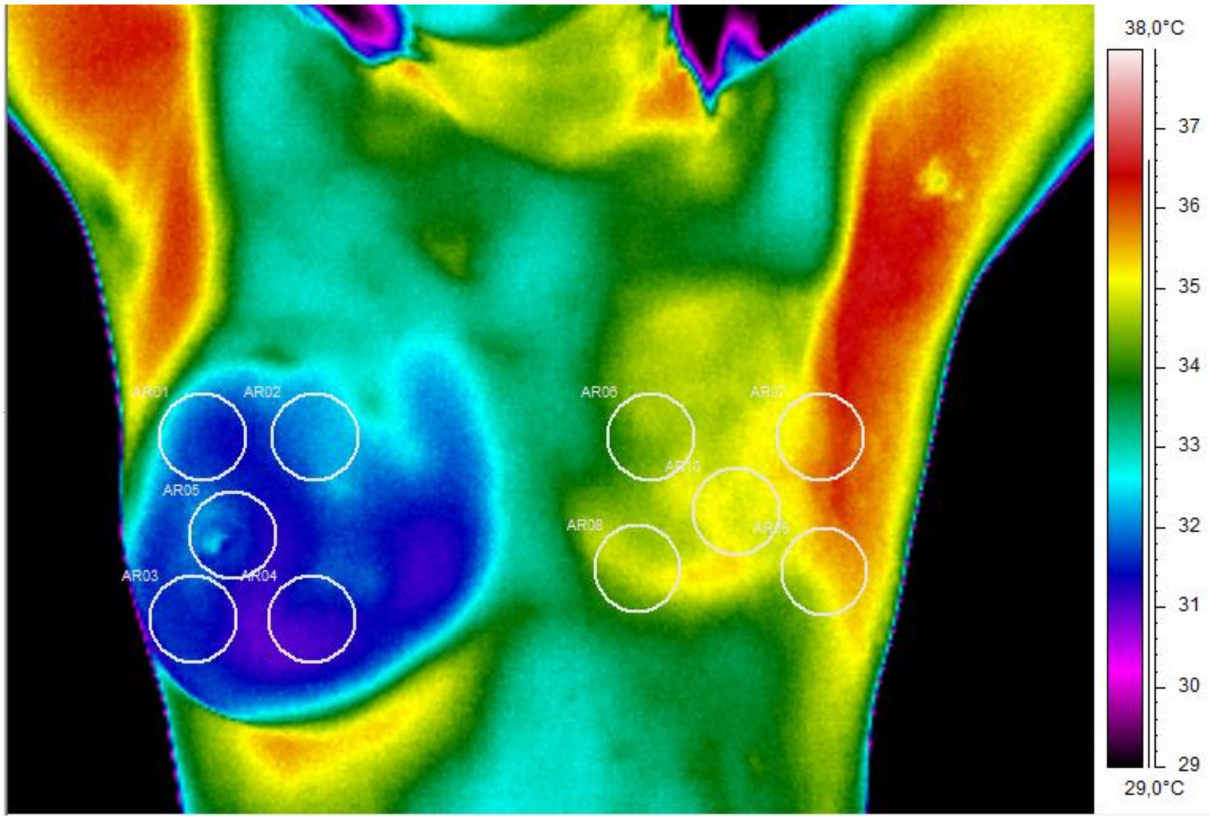


Figure 4.3.5: Establishment of ROI's.

Table 4.13 - Collection environmental conditions

PHASE COLLECTION	COLLECTION TIME	TEMPERATURE (°C)	RELATIVE HUMIDITY (%)
PRE-OPERATIVE	Previous day of surgery	22	52.3
INTRA-OPERATIVE	Day of surgery	20.8	56.1
POST-OPERATIVE	4 days after surgery	22.7	53.1

4.3.4. Results of pre-operative phase

The selected ROI'S for analysis of mean temperature value at skin surface of breast are exposed in next thermogram (figure 4.3.6) and the results are expressed in table 4.14. The thermogram of flap is presented in figure 4.3.7 and the temperature value is registered in table 4.15.

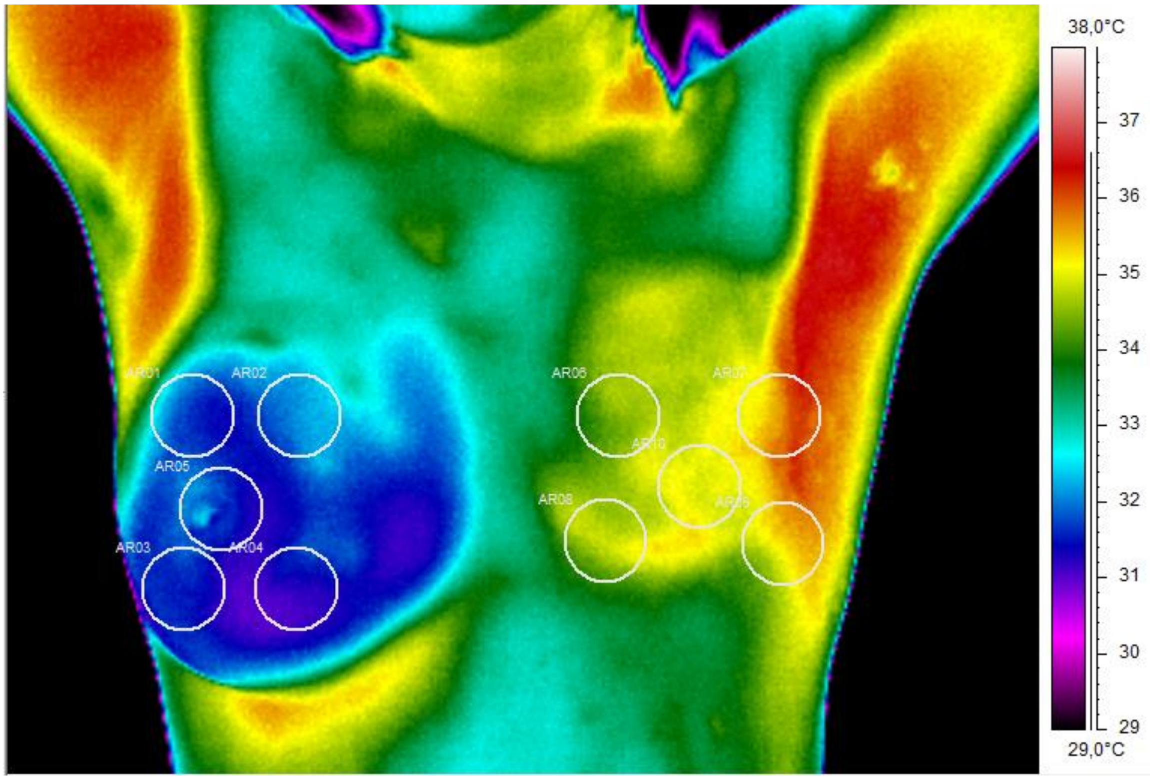


Figure 4.3.6: Thermal image of four quadrants of breast selected and nipple.

Table 4.14 - Analysis of ROI's of pre-operative phase

ROI'S	MEAN TEMPERATURE (˚C)	MAX TEMPERATURE (˚C)
RESQ (AR01)	31.9	33.4
RISQ (AR02)	32.1	32.7
REIQ (AR03)	31.6	32
RIIQ (AR04)	31.3	31.9
NR(AR05)	31.7	32.5
LISQ (AR06)	34.5	35
LESQ (AR07)	35.7	36.5
LIIQ (AR08)	34.7	35.3
LEIQ (AR09)	35.2	35.9
NL(AR10)	35.1	35.3

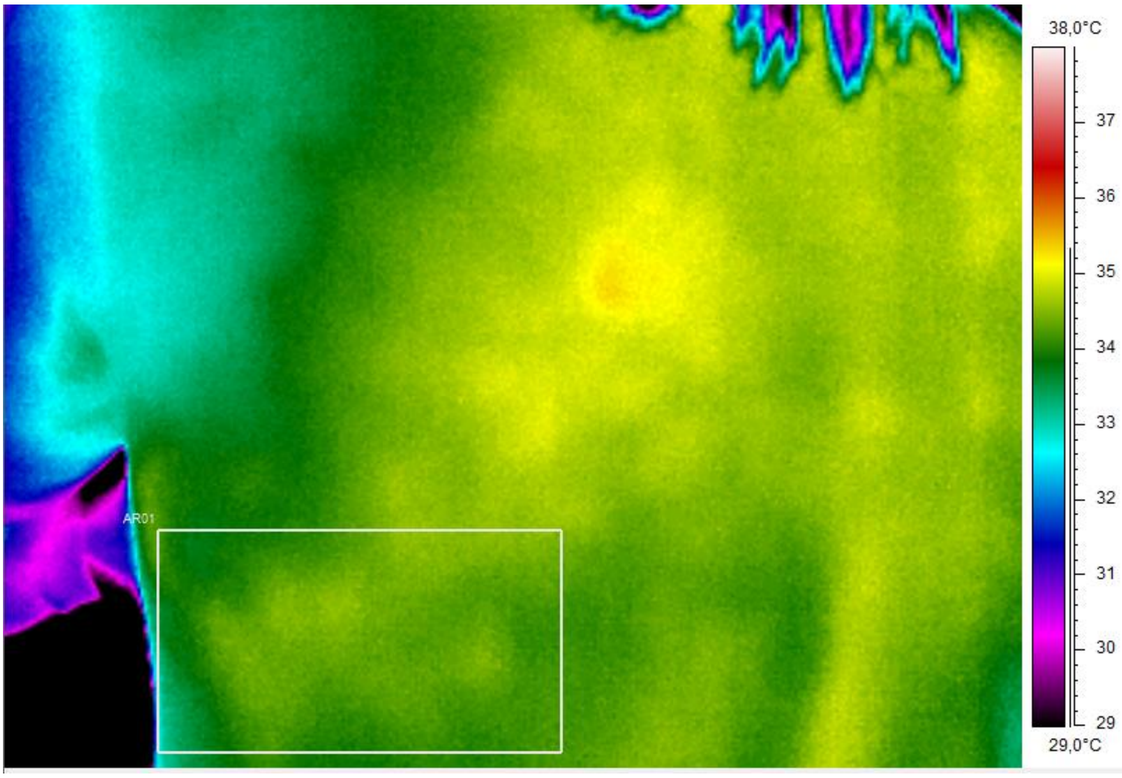


Figure 4.3.7: Thermal image of flap selected, *Latissimus dorsi* muscle.

Table 4.15 - Analysis of ROI (flap) of pre-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	34.2	34.7

4.3.5. Results of intra-operative phase

During the surgery, there were captured the thermal images of flap lifting before the reconstruction has been completed. The digital image is exposed in image 4.3.8 and its thermal image is presented in figure 4.3.9. The results of ROI selected in this image is presented in table 4.16.

Figure 4.3.8: Digital image of flap selected *Latissimus dorsi* muscle at intra-operative phase.

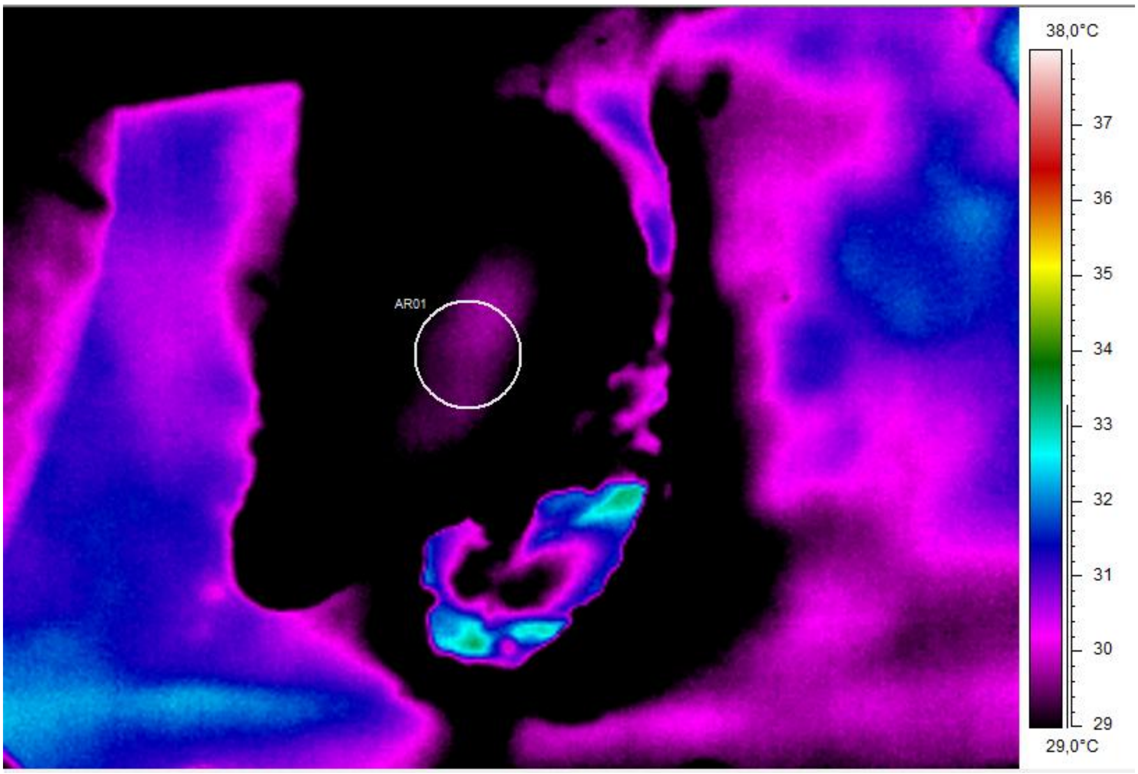


Figure 4.3.9: Thermal image of flap selected, *Latissimus dorsi* muscle at intra-operative phase during to lifting of tissue.

Table 4.16 - Analysis of ROI (flap) of intra-operative phase during to flap lifting

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	29.4	29.9

In figures 4.3.10 and 4.3.11 are presented the digital image and thermogram correspondent of flap after this has been sutured in breast, completing the autologous breast reconstruction. The results of this thermogram is expressed in table 4.17.

Figure 4.3.10: Digital image of flap selected, *Latissimus dorsi* muscle at intra-operative phase.

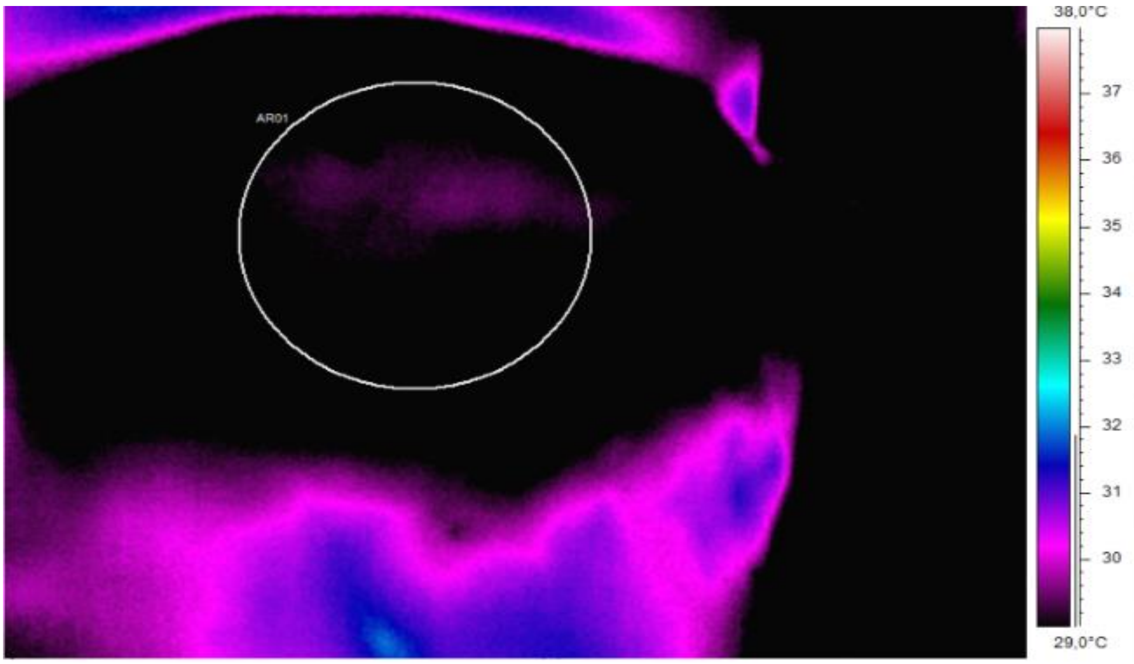


Figure 4.3.11: Thermogram of flap selected, *Latissimus dorsi* muscle at intra-operative phase.

Table 4.17 - Analysis of ROI (flap) at intra-operative phase in the end of intervention

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	28.7	29.6

Through analysis of data exposed in the previous tables, it is possible to observe lower temperatures values at flap comparing with the values obtained at the pre-operative period.

4.3.6. Results of post-operative phase

The collection of images referring to post-operative phase was performed at 4 days after breast reconstruction. The digital image and thermogram after intervention are presented in figures 4.3.12 and 4.3.13.

Figure 4.3.12: Digital image of breast quadrants at post-operative phase.

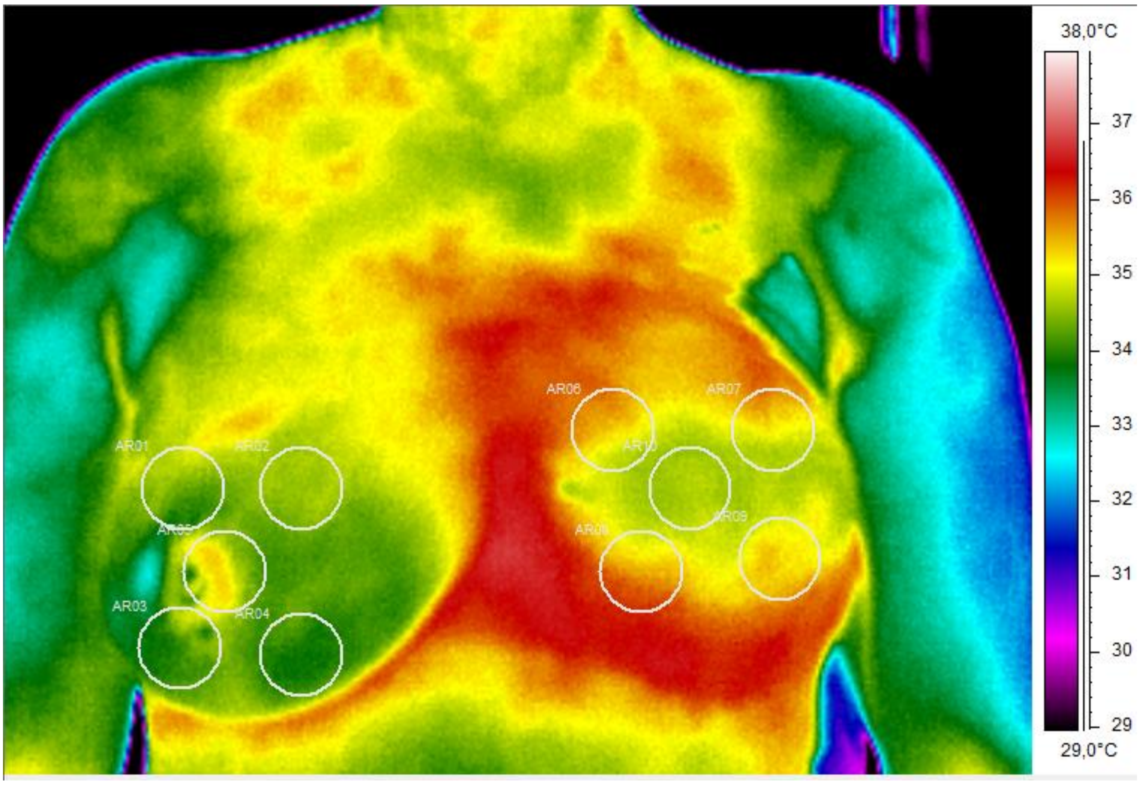


Figure 4.3.13: Thermal image of four breast quadrants and nipple at post-operative phase.

The data of different breast quadrants are presented in table 4.18. The thermal symmetry between two breasts is presented in table 4.19.

Table 4.18 - Analysis of ROI's of post-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
RESQ (AR01)	34.4	35
RISQ (AR02)	34.5	34.8
REIQ (AR03)	34.2	35.1
RIIQ (AR04)	34.1	34.4
NR(AR05)	34.8	35.5
LISQ (AR06)	35	35.7
LESQ (AR07)	35.1	35.9
LIIQ (AR08)	35	36
LEIQ (AR09)	35.3	35.9
NL(AR10)	34.7	35

Table 4.19 - Differences of temperature between quadrants of breasts

Breast Quadrants	ΔT value (T of right breast-left breast)
ESQ	-0.7
ISQ	-0.5
EIQ	-0.8
IIQ	-0.9
Nipple	0.1

4.3.7. Discussion of case 3

The patient of this study does not had the left breast, which was removed in 2015. For the study of temperature values in pre-operative phase, there were established the ROI's in side without breast similarly to the location in the right breast. The temperature values of right breast ROI's are within the interval [31.3-32.1] °C and the interval of left side is [34.2-35.7] °C. In the left side was observed temperatures significantly higher than right side. This increase of temperature values for mastectomized breast can be justified due to the fact that this zone presents a lower adipose layer, consequently, less resistance to the heat and therefore an increase of energy release by radiation, translating into a general increase of the skin temperature captured by thermal camera. The temperature of flap was 34.2°C, this value is close to the temperature values of left breast.

At the intra-operative phase, there were collected thermal images in two steps: first at the lifting of flap and secondly in the end of surgery procedure. The both thermal images collected during the surgery cannot provide safe results because skin surface was covered with disinfectant substances.

The results of post-operative phase demonstrate that for right breast, there was an increase of mean temperature value of ROI's with interval of [34.1-34.5]°C reveling temperature values very similar ROI's for the same breast. For left side, there was slight increase of temperature for different ROI's. For this study case, it was not possible to study the temperature values of healing points for healing process monitoring because in data collections at post-operative phase, because the patient contained medical dressings. However, with these data, it was possible to conclude that the surgery presents good indicators of adequate healing process and good blood supply of flap, which corresponds to the clinical outcomes, that were considered favorable.

According to ΔT mean value less than 1, it is possible to affirm that the breasts presented a good postoperatively thermal symmetry. Also at post-operative phase, the left breast presented a higher temperature value than right breast, such as in pre-operative phase. Similar to previously case, the breast reconstructed presents higher temperature than contralateral breast and this aspect can be justified by the healing process associated to tissue suturing procedure. With the analysis of the thermal images in post operatory phase, it is not visible any complication associated to reconstructed breast, situation that was confirmed by clinical information of the patient.

4.4. Case of Study 4

4.4.1. Description of case

The case of study 4 has study a woman with 50 years and BMI of 24.24 kg/m^2. This patient has a history of breast cancer, particularly on the left side, diagnosed in 2010. At that time, she underwent lumpectomy and axillary emptying, chemotherapy, radiation therapy, hormone therapy, and Herceptin (monoclonal anti-body). This woman has a genetic mutation, BRCA1+.

In this study, the patient undergone to total mastectomy of the left breast and prophylactic mastectomy to the right side. The reconstruction was made by the use of free DIEP flap for both breasts. The figure 4.4.1 shown the breasts before the intervention.

Figure 4.4.1: Digital image of breasts at pre-operative phase.

4.4.2. Flap Selection

The selected flaps for this reconstruction were free DIEP flaps. The choice is due to the bilateral breast reconstruction, which requires a greater amount of tissue and this area is the most appropriate for patient. In figure 4.4.2 is exposed the digital image of flaps used for breasts reconstruction and marked with small circles, the flap perforators detected by Doppler technique.

Figure 4.4.2: Digital image of DIEP flap in pre-operative phase.

4.4.3. Aim, Methods, and Collection Conditions

In this study case, there is a use of free DIEP flap for breast reconstruction. This type of reconstruction requires that an anastomosis be performed during surgery in which the main artery of the flap is attached to the arteries of the breast. It is therefore very important to accurately locate the perforators of the flap. As mentioned in literature review, the thermography has an important role in this detection. The aim of this case study is to check whether thermography is an effective technique for locating these perforators at the pre-operative phase. In addition, it is intended to monitor the healing process of the reconstruction.

The images (digital and thermal) were collected at pre, intra and post-operative phases. The static analysis was performed in order to compare the temperature values of respective ROI’s between pre, and post-operative phases. The ROI’s selected for analysis to compare the data were four breast quadrants around the nipple, similar to the previous two case studies. The ROI’s selected are shown in the figure 4.4.3. The methodology used for evaluating the temperature of breasts at pre, and post operative phases was the static thermography. For the evaluation of temperature of perforators, was performed the DIRT technique using a metal plate described in detail in section 3.3.2 (dynamic study). The ROI’s for this goal was defined according to localization of flap perforators detected by Doppler demonstrated in figure 4.4.4. In this figure the orange circles correspond to area of two perforators detected by Doppler. The other circles correspond to metal pieces to indicate the perforators localization. These results were the references for the dynamic study. The collection environmental conditions are exposed in table 4.20. Similarly, to the other cases, it was intended to monitor the healing process.

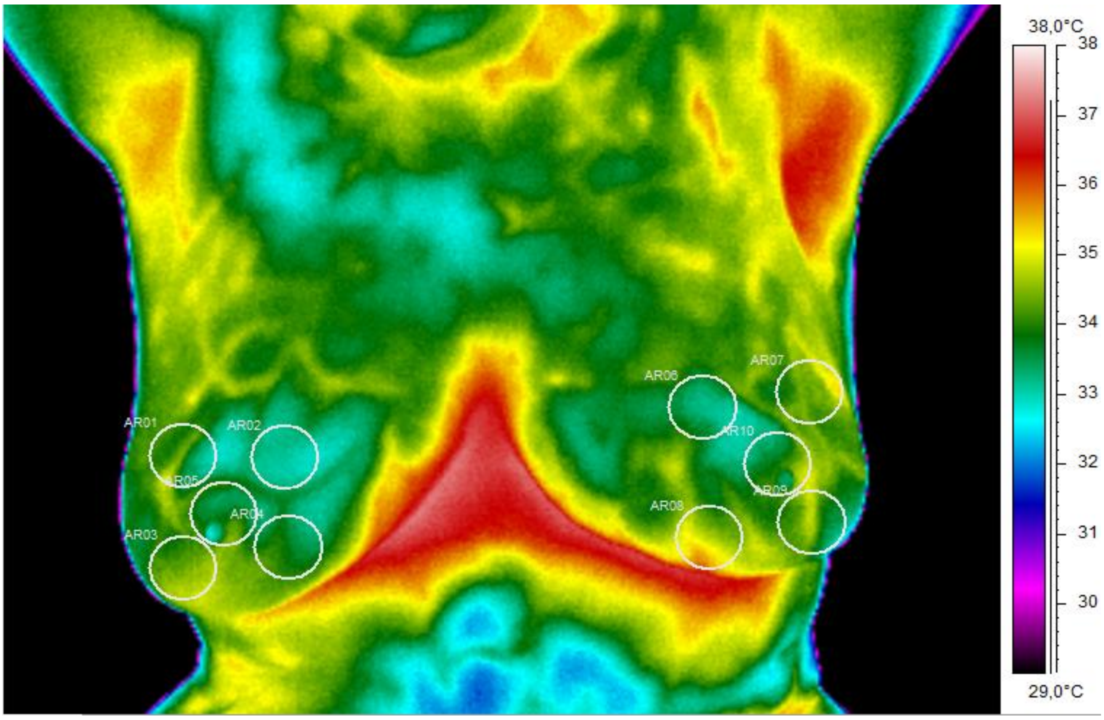


Figure 4.4.3: ROI’s selected.

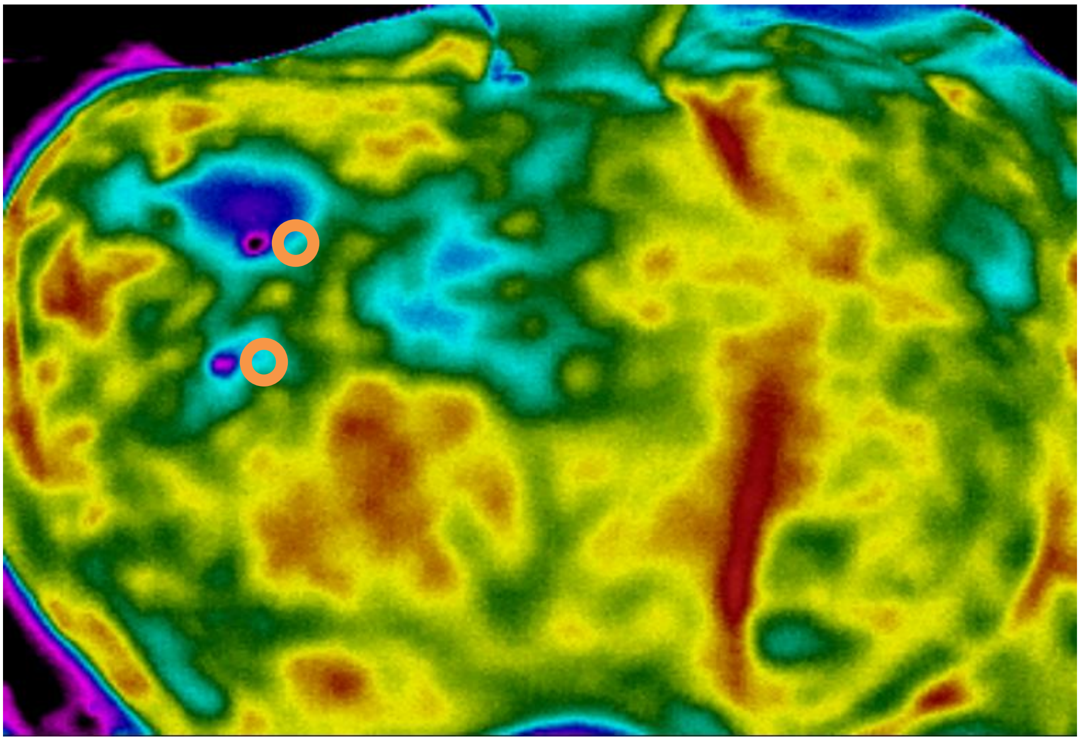


Figure 4.4.4: Establishment of flap ROI’s (perforators).

Table 4.20 - Collection environmental conditions

PHASE COLLECTION	COLLECTION TIME	TEMPERATURE (°C)	RELATIVE HUMIDITY (%)
PRE-OPERATIVE	Previous day of surgery	25.9	59.5
INTRA-OPERATIVE	Day of surgery	21	55.4
POST-OPERATIVE	1 days after surgery	23.1	52.9

4.4.4. Results of pre-operative phase

The selected ROI'S for static analysis of mean temperature value at skin surface of breast are exposed in the thermogram of figure 4.4.5 and the results of pre-operative phase are expressed in table 4.21.

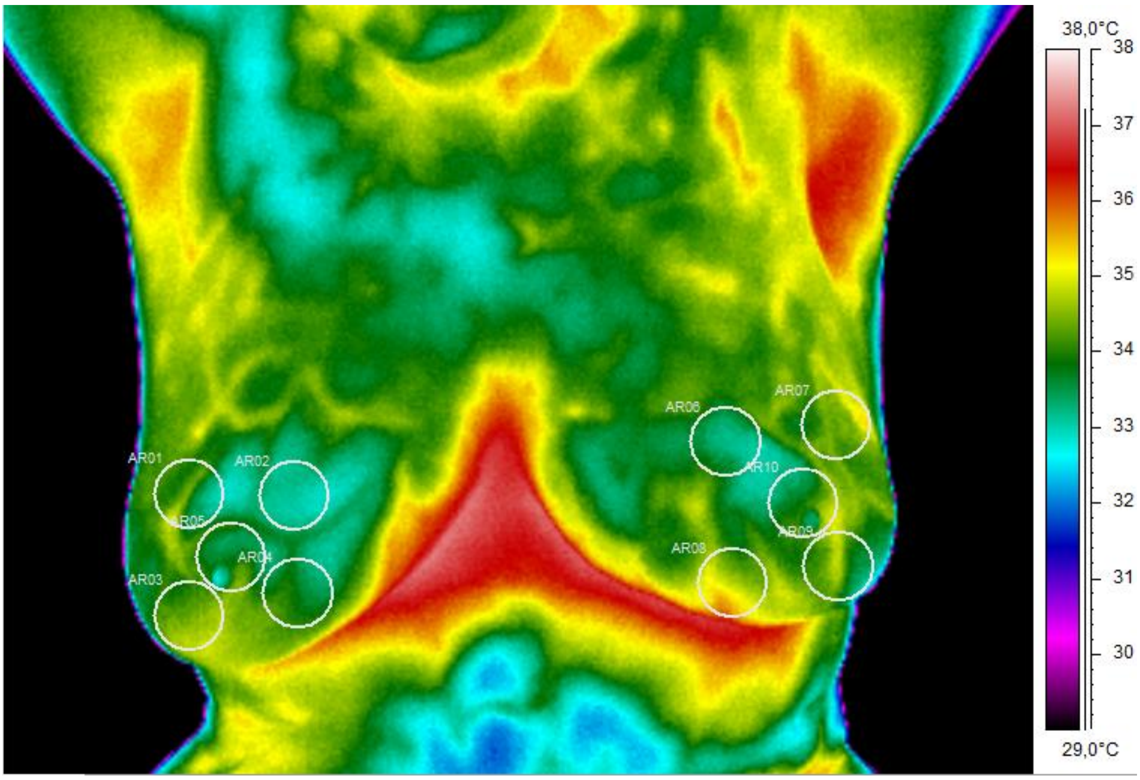


Figure 4.4.5: Thermal image of four quadrants and nipple of breast at the pre-operative phase.

Table 4.21 - Analysis of breast ROI's at the pre-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
RESQ (AR01)	34.1	35
RISQ (AR02)	33.3	33.9
REIQ (AR03)	34.3	34.9
RIIQ (AR04)	33.5	34.8
NR(AR05)	33.8	34.7
LISQ (AR06)	34.3	34.5
LESQ (AR07)	34.2	35.4
LIIQ (AR08)	34.6	35
LEIQ (AR09)	33.9	35.1
NL(AR10)	34	35

The mean temperature value of flap is registered in table 4.22 and the select ROI is demonstrated in figure 4.4.6.

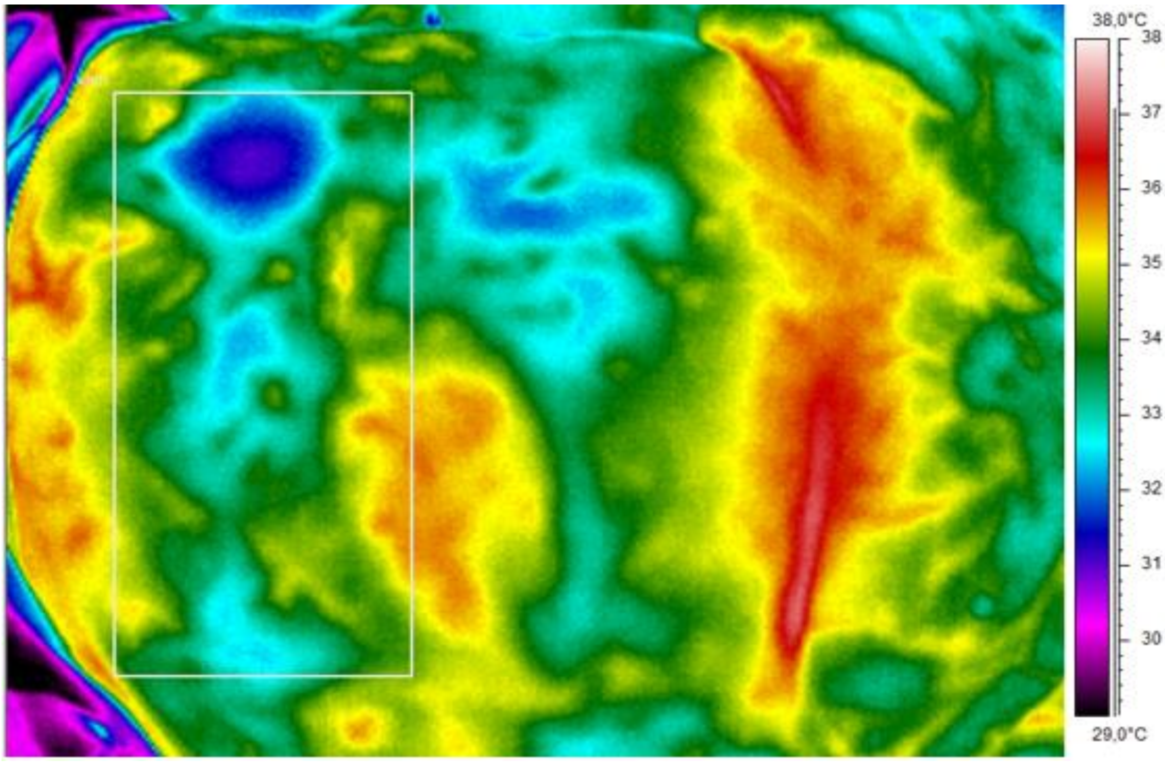


Figure 4.4.6: DIEP flap.

Table 4.22 - Analysis of ROI (flap) at the pre-operative phase

ROI'S	MEAN TEMPERATURE (°C)	MAX TEMPERATURE (°C)
FLAP (AR01)	33.7	35.9

Some thermal images of perforators study are presented in the figure 4.4.7 and mean temperature values of two selected perforators before and after thermal stimulation are exposed in table 4.23. The 0 minutes corresponds exactly at moment of the stimulus is removed.

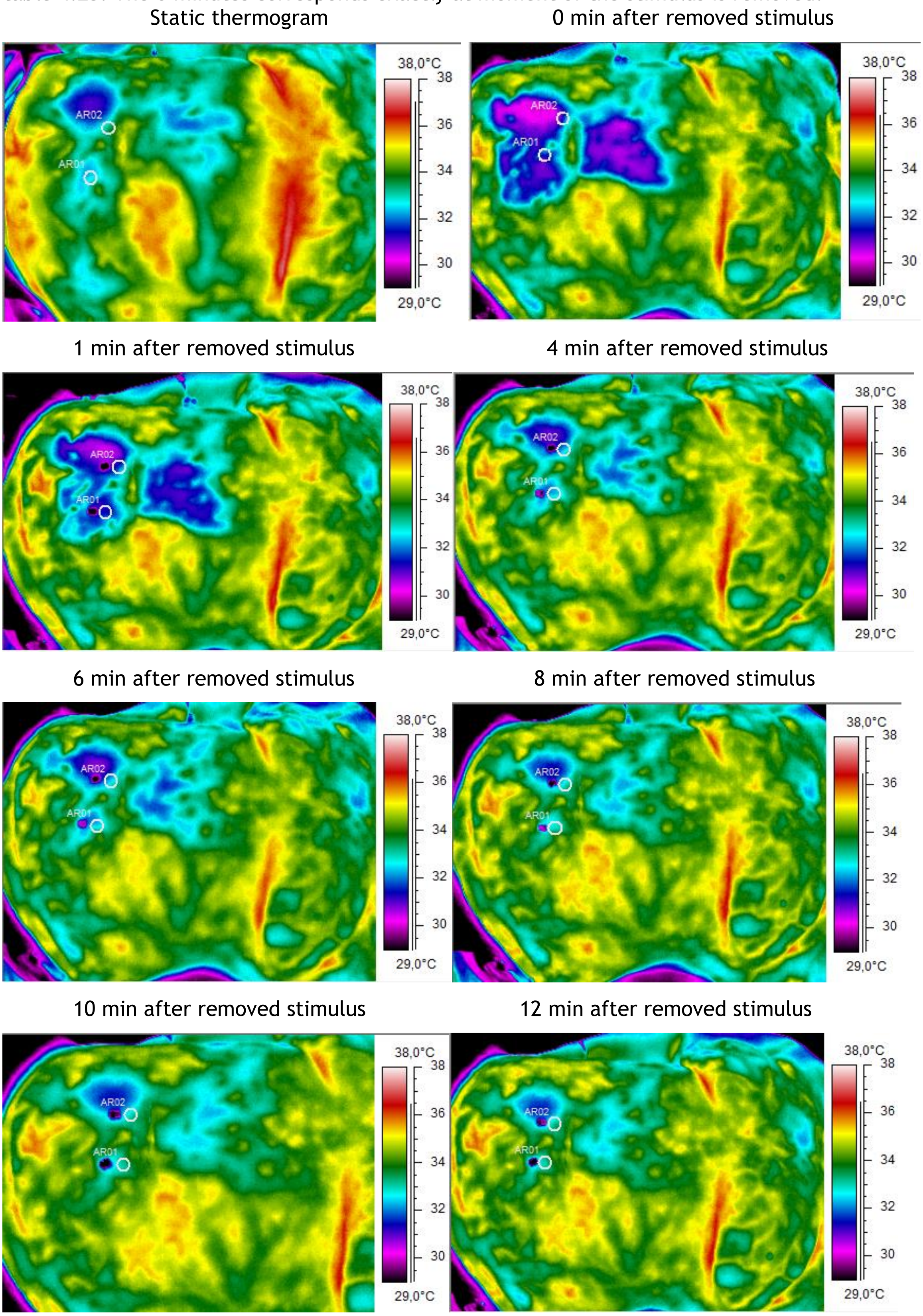


Figure 4.4.7: Set of thermal images of DIRT on the perforators identification.

Table 4.23 - Analysis of perforators ROI's at the pre-operative phase

ROI'S	PERFORATOR 1(AR01)	PERFORATOR 2(AR02)
STATIC	32.9	33.3
0 MIN	31.6	31.6
1 MIN	31.6	31.8
2 MIN	31.8	32
3 MIN	32	32.1
4 MIN	32.6	32.4
5 MIN	32.7	32.5
6 MIN	32.8	32.6
7 MIN	33.1	32.9
8 MIN	33.2	33
9 MIN	33.2	33
10 MIN	33.2	33
11 MIN	33.2	33.1
12 MIN	33.2	33.1

For better comprehension, it was elaborated a graphic with temperature evolution over time for two identified main perforators. This graphic is exposed in the figure 4.4.8.

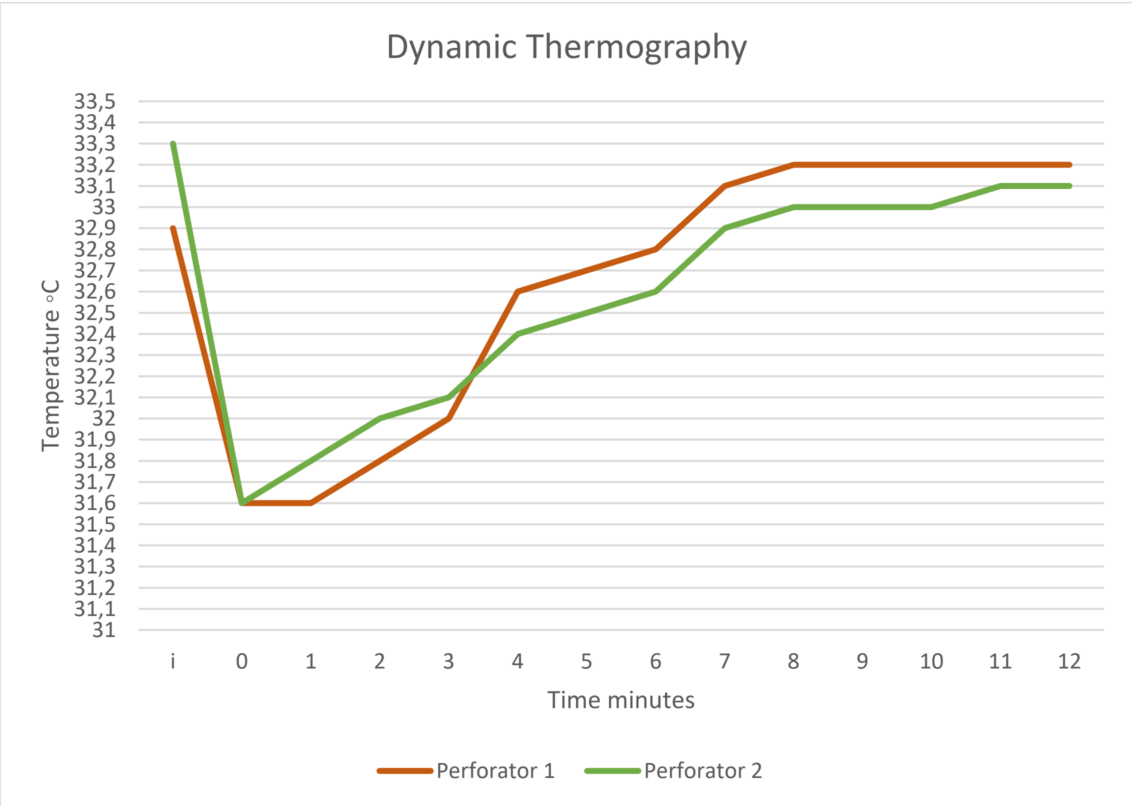


Figure 4.4.8: Chart of temperature evolution over time for two perforators.

4.4.5. Results of intra-operative phase

During to breast reconstruction, there was captured the thermal image at the end of surgery. But in this case, the thermal image cannot provide relevant data because the flap was placed behind the mammary skin, not being on the surface preventing it from being monitored. In figure 4.4.9 and 4.4.10 are presented the digital images at intra-operative phase and thermogram, respectively.

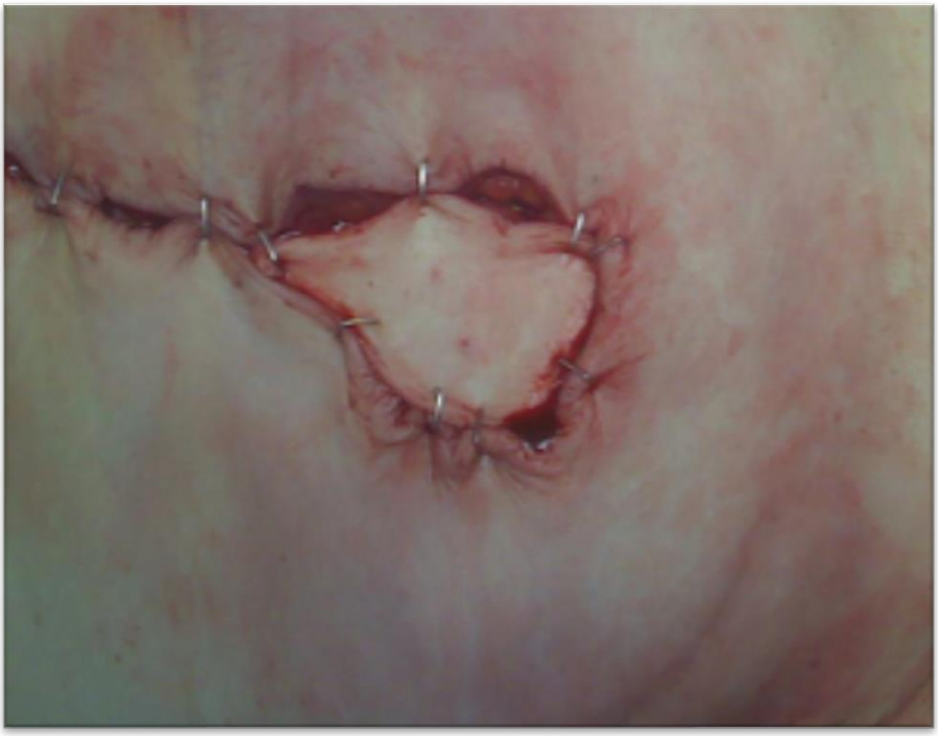


Figure 4.4.9: Digital image of breast at the end of the intra-operative phase.

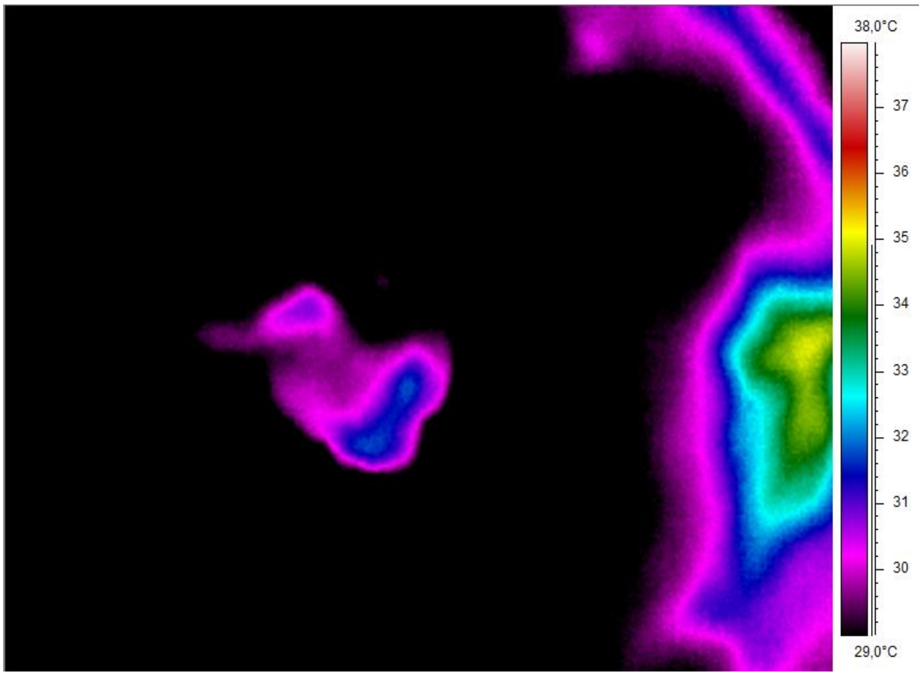


Figure 4.4.10: Thermal image of breast at the end of the intra-operative phase.

4.4.6. Results of post-operative phase

As noted before, because the flap was placed behind the skin of the breast and not at the surface, it does not allow the ROI's to be analyzed. Also for this reason, it is not possible to monitor the reconstructed breast healing process. This thermal image is impossible to analyze, consequently it is not possible compare the temperature value of both breast quadrants between pre and post-operative phases, and it is impossible to determine the thermal symmetry after surgery. The images collected at post-operative phase are exposed in figure 4.4.11 and figure 4.4.12.

Figure 4.4.11: Digital image of breast at post-operative phase.

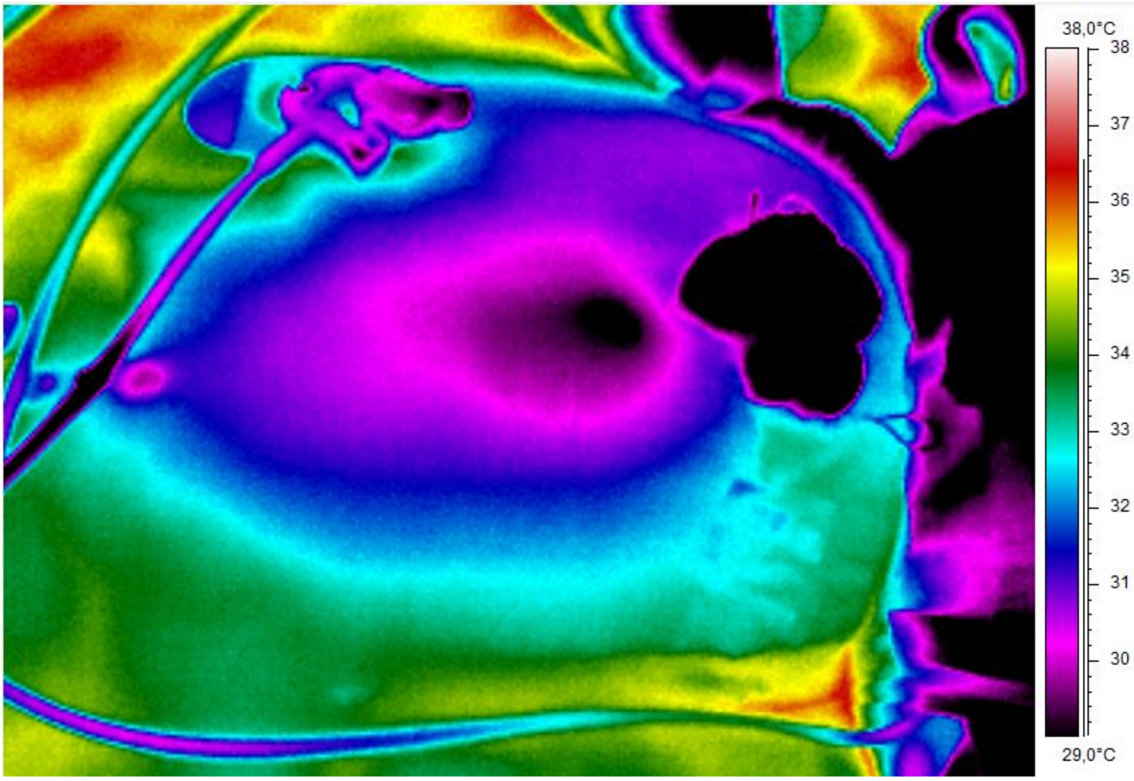


Figure 4.4.12: Thermal image of breast at post-operative phase.

4.4.7. Discussion of case of study 4

According to the data obtained at the pre-operative phase, the ROI's presented different mean temperature values. In right breast, the interval of mean temperatures was [33.3-34.3]°C. In left breast, the mean temperature values were close of right breast and interval was [33.9-34.6]°C. In right side, the intern quadrants were those with lower temperatures. Contrary, in left side, the extern quadrants had lower temperatures. The DIEP flap obtained a mean temperature value of 33.7 °C which is within the quadrants range of both breasts.

In the dynamic study, it was used an external thermal challenge through contact method, the metal plate was applied in direct contact for 1 minute. At the pre-operative phase, there were collected thermal images before and after stimulation. At the basal thermogram, the temperature of the two perforators (ROI's established according to localization of perforators arteries detect with Doppler) was 32.9 °C and 33.3 °C, respectively for perforator 1 and perforator 2. At the exact moment after the stimulus was removed, the temperature recorded for the perforators was 31.6°C for both. So, it is possible conclude that the metal plate caused an uniform and effective cooling with the contact zone. Over time the area had become warmer and the temperature value of the perforators increased. However, the perforator 1 was able to reach the temperature of the basal thermal image between minutes 6 and 7 and reached a higher value in the following minutes. Looking at the chart of the figure 4.4.8, it can be verified that after reaching the temperature near the basal, from that point there was no evolution of the temperature, it remained in constant values. These results thus demonstrate that perforator 1 had a complete thermal recovery after thermal challenge as expected.

Contrary, the perforator 2 did not reached the basal temperature but also presented a partial thermal recovery, stabilizing after 11 minutes.

One of the most important objectives of this study, in this phase was the identification of the appearance of hot spots after external thermal stimulation for the detection of the main perforators of the flap. These results would be compared with those obtained through Doppler, which served as a reference. In this case of study, it was not possible to distinguish any hot spot from the stimulated area near the points that were detected by Doppler. In the figure 4.4.7 of the dynamic study it is not possible distinguish two points with a higher temperature than the surrounding zone and near the marks performed by Doppler that allows to verify the existence of possible perforators. Thus, in contradiction with the published studies by Weerd, Mercer, and Weum [9], Zetterman *et al.* [150] and Salmi, Tukiainen, Asko-Seljavaara [184], and Theuvenet *et al.* [187] the perforators were not detected and identified using dynamic thermography. Majority of studies of Weerd and colleagues [9,188] in which good results were obtained, a different external thermal stimulation method, convection method (cooling fan), was used. According to a previous study performed in this research, the metal plate demonstrated to be more efficient in cooling. Furthermore, the contact method does not present the disadvantages that the convection method has such as: there is no risk of undesirable dispersion of microorganisms in a hospital environment and does not cause directional differential cooling. These were the main reasons that led to the choice of contact method. However, in this study, other methods were not testes, which may have an influence on the obtained results.

It is important to note that these results are just from one patient and it makes it impossible to conclude that the dynamic thermography was not efficient using this method. A bigger sample is necessary to measure the effectiveness of dynamic thermography in perforator detection using the proposed approach.

The intra and post-operative static analysis is rudimentary and does not allow the obtention of significant and interesting data for the research. The flap is not accessible at skin surface and so is not possible to study the adequate anastomosis at the intra-operative time and healing process at the phase of post-surgery.

To conclude, the patient presented clear clinical recovery demonstrating the success of the surgery.

4.5. Case of Study 5

4.5.1. Description of case

This case of study examines the application of static infrared thermography in a burn. The patient has 31 years and a BMI of 23.38 kg/m^2. He was a victim of an electronic cigarette explosion in his pocket and resulted in a thigh burn in left side on 9 July at 11 p.m.

4.5.2. Aim, Methods, and Collection Conditions

In this case study, it is intended to study the effectiveness of thermography to detect the type of burns: superficial, partial thickness, full thickness and deep. For this, it was compared the classification of burns by clinical evaluation to the results of static thermography based on the difference value of temperature between burned area and unburned area (ΔT) which is documented in literature review. The collected environmental conditions are showed in the table 4.24.

Table 4.24 – Collection Environmental Conditions

COLLECTION	COLLECTION TIME	TEMPERATURE (°C)	RELATIVE HUMIDITY (%)
SINGLE COLLECTION	After 36 hours of burn	24.6	56

4.5.3. Results

As before mentioned, in this case, a comparison between the diagnostic by clinical evaluation performed by plastic surgeon with the results obtained by thermographic camera is assessed.

Clinical evaluation

In figure 4.5.1. is exposed the digital image of burn. For analysis, was selected ROI's classified by clinical evaluation and will be the reference for analysis of thermography.

Figure 4.5.1: Digital image of burn with ROI's.

According to clinical evaluation the AR01 is considered a burn of IIa degree, superficial partial thickness because it is a red zone and it is not too deep. The AR02 zone was classified as IIb degree, deep partial-thickness burn presenting a less reddish color.

Thermography

The thermographic analysis of the ROI's were same of clinical evaluation and were selected areas in correspondent unburned contralateral area to the burned area. The thermograms of unburned and burned thighs are exposed in figure 4.5.2. and figure 4.5.3 respectively. The results of mean temperature of ROI's in both the areas are expressed in table 4.25.

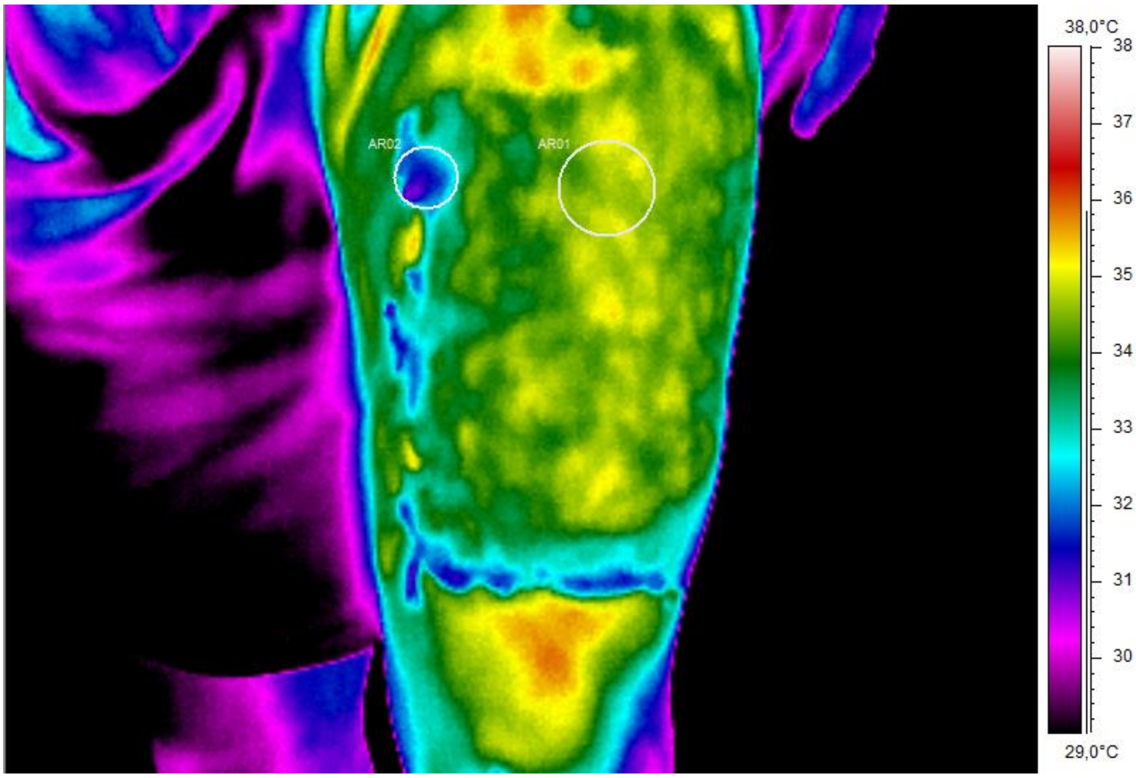


Figure 4.5.2: Thermal image of burn with ROI's at burned area.

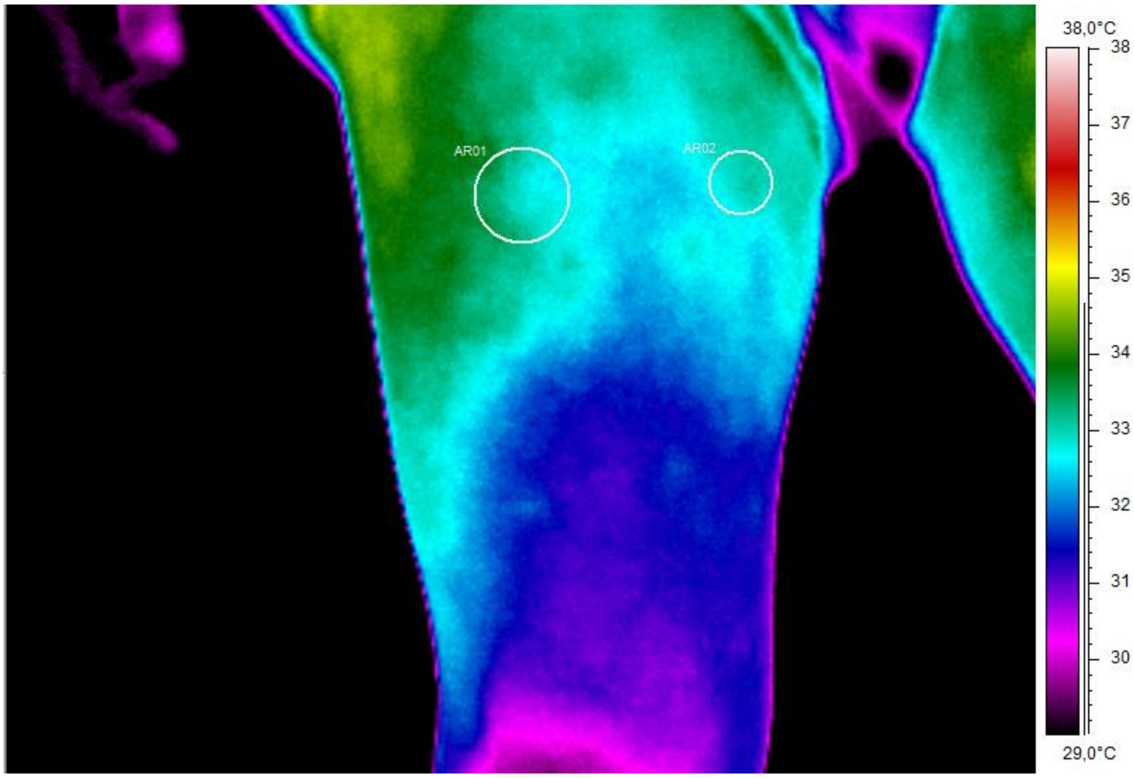


Figure 4.5.3: Thermal image of burn with ROI's at unburned area.

Table 4.25 – Results of thermogram analysis of burns

ROI'S	BURNED THIGH TEMPERATURE (BT)	UNBURNED THIGH TEMPERATURE (UT)	ΔT=(BT-UT)
AR01	34.7	33.1	1.6
AR02	32.1	32.9	-0.8

4.5.4. Discussion of case of study 5

According to the literature, thermography has used as auxiliary method for burn depth classification. In case of burns, is important to refer that the time of thermal image collection cannot exceeded 48 hours after injury.

To assess whether thermography is an effective method for burn depth assessment, it was compared the outcome of clinical evaluation with the difference of mean temperatures between burned area and contralateral unburned area.

The burned area may have different depths. In the studied case, the area is extense and has different depths. Two ROI's were selected in which depth was known from the clinical evaluation made by the surgeon. According to the clinical method, the ROI AR01 was classified as IIa degree, superficial partial thickness burns and the ROI AR02 was classified as IIb degree, deep partial-thickness burn. These ROI's were selected in the thermograms to obtain the mean temperature values in burned tissue and contralateral unburned tissue.

For the ROI AR01, it was obtained a ΔT mean value of 1.6 °C, with the affected tissue having a higher temperature than healthy tissue. This result is in agreement with the documented studies, such as: study of Zhu and Xin [259] reported that for superficial partial skin thickness (II°a) the temperature was in general higher than that of the contralateral unburned skin and according to Medina-Preciado *et al.* [253], for superficial dermal (II°a), an average ΔT of 1.7°C was presented with an increased temperature when compared to their contralateral healthy region. Given that, thermography had accurately assessed the burn depth for this selected ROI (AR01), which corresponded to the classification of clinical evaluation.

The ROI AR02 presented a ΔT mean value of -0.8 °C, demonstrating that the burned tissue is colder than the unaffected contralateral area. Through this observation, it is possible to conclude that this zone has a depth greater than the region AR01 because they have damaged blood vessels and therefore it has a lower temperature, since thermography does not detect as much heat at the surface of the skin. This result is supported by literature and according to Hardwicke *et al.* [252] deep partial thickness burns were 1.2 °C cooler that unburned contralateral skin area (ΔT=-1.2°C). The value obtained in this case study is close, being possible to state that thermography determined correctly the burn depth. Despite being only a single case result, the method proved to be a valid complementary technique for burn depth assessment.

Chapter 5

Conclusion and Future Work

Thermography has been previously studied as an effective adjunctive modality in plastic and reconstructive surgery, however in Porto hospitals it was not yet previously tried. In plastic surgery and specifically in breast reconstruction, DIRT can be used to identify perforators in planning flap reconstruction and perforator selection, intraoperatively to assess perfusion and postoperatively for flap monitoring. Ideally the flap monitoring needs to be non-invasive, free of side effects, reliable, rapid, repeatable, accurate, painless, and easy to operate. The benefits of DIRT have been demonstrated and the data suggest that DIRT is a useful adjunct to current techniques to map and characterize perforators in flaps. In the other hand, in case of unavailable techniques such as CTA and MCDT, DIRT can be used as an alternative reducing the exposure to ionizing radiation for patients.

The proposed aim of this research was satisfied. From it there was possible to conclude that this technique proved to be useful as a complementary method for the monitoring of the thermophysiological alterations essential postoperatively in breast reconstruction, the thermal symmetry was studied in healthy women breasts and reference values of temperature difference in different regions of the breast were obtained. In burns, it proved to be a reliable method for burn depth assessment. However, an proposed objective did not present satisfactory results, it was the dynamic thermography applied to the detection of flap perforators.

For future work, it would be interesting to define and test other dynamic thermography methodologies for detecting the main perforators. Another optimization of this work would be to consider employing static thermography and dynamic thermography in flaps, and static thermography in burns, in larger significant samples.

In plastic surgery, DIRT has not yet been widely used in comparison with other imaging technologies to confirm its reliability in breast reconstruction. Despite the appropriate skills survival of flaps, necrosis complications occur and have significant consequences, which could be reduced.

This dissertation may have been the starting point for new investigations with optimization of methodologies in plastic and reconstructive surgery, since it was a pioneer in Portugal.

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Appendixes

Appendix I: Ethics committee authorization

Unidade de Investigação

Tomei conhecimento. Nada a opor.

22 de Março de 2017

A Coordenadora da Unidade de Investigação

(Prof.ª Doutora Ana Azevedo)

DIRECÇÃO CLÍNICA

Aprovado. Ao CA. 22/3/2017

(Prof.ª Doutora Ana Azevedo)

56-17

AUTORIZADO

23 MAR 2017

Exmo. Senhor

Presidente do Conselho de Administração do

Centro Hospitalar de S. João – EPE

Assunto: Pedido de autorização para realização de estudo/projecto de investigação

Nome do Investigador Principal: Diana Filipa Passos Dias Marques de Abreu

Título do projecto de investigação: Caracterização térmica de retalhos utilizados em cirurgia plástica e reconstrutiva.

Pretendendo realizar no(s) Serviço(s) de Cirurgia Plástica, Reconstrutiva e Unidade de Queimados do Centro Hospitalar de S. João – EPE o estudo/projecto de investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efectivação.

Para o efeito, anexa toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar de S. João respeitante a estudos/projectos de investigação, à qual endereçou pedido de apreciação e parecer.

Com os melhores cumprimentos.

Parecer da Comissão de Ética para a Saúde do
Centro Hospitalar de São João / Faculdade de Medicina da Universidade do Porto

Titulo do Projecto: Caracterização térmica de retalhos utilizados em Cirurgia Plástica e Reconstrutiva

Nome da Investigadora Principal: Eng.ª Diana Filipa Passos Dias Marques Abreu

Onde decorre o Estudo: No Serviço de Cirurgia Plástica do CHSJ. Apresentou declaração do Dr. Álvaro Silva, que se apresentou também como profissional de ligação.

Objectivos do Estudo:
Estudar e caracterizar termicamente os retalhos utilizados na reconstrução mamária em mulheres mastectomizadas. Para tal, utilizar-se-á a técnica da termografia. O estudo contempla análises pré-operatórias, intra-operatórias e pós-operatórias de forma a realizar um acompanhamento rigoroso do doente.
Este estudo insere-se no âmbito do Mestrado em Engenharia Biomédica da FEUP, sob orientação do Doutor Ricardo Ângelo Rosa Verdasca.

Beneficio/risco: N/A

Confidencialidade dos dados:
Nos questionários realizados não serão incluídos dados que permitam identificar os participantes, sendo que serão apenas identificados por números.

Respeito pela liberdade e autonomia do sujeito de ensaio: Está garantida a obtenção de um consentimento informado, livre e esclarecido, complementado por uma informação para o participante, onde constam os objetivos, benefícios e eventuais riscos, bem como a liberdade em participar.

***Curriculum* da investigadora**: Adequado à investigação.

Data previsível da conclusão do estudo: Junho 2017

Conclusão: Proponho um parecer favorável à realização deste projecto de investigação.

Porto, 17 de Fevereiro de 2017

O Relator da CES, Dr. John Preto

CES

COMISSÃO DE ÉTICA PARA A SAÚDE

Pelos danos resultantes da sua participação no estudo ☐ ☐ ■

7. **SEGURO**

a. *Este estudo/projecto de investigação prevê intervenção clínica que implique a existência de um seguro para os participantes?*

SIM ☐ (Se sim, junte, por favor, cópia da Apólice de Seguro respectiva)

NÃO ☐

NÃO APLICÁVEL ■

8. **TERMO DE RESPONSABILIDADE**

Eu, Diana Filipa Passos Dias Marques de Abreu, abaixo-assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (com as emendas de Tóquio 1975, Veneza 1983, Hong-Kong 1989, Somerset West 1996 e Edimburgo 2000) e da Organização Mundial da Saúde, no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo no decurso do actual internamento ou da mesma consulta.

Porto, Dezembro de 2016

O Investigador Principal

PARECER DA COMISSÃO DE ÉTICA PARA A SAÚDE DO CENTRO HOSPITALAR DE S. JOÃO/FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO

emitido na reunião plenária da CES de 12 / Fevereiro / 17

A Comissão de Ética para a Saúde APROVA por unanimidade o parecer do Relator, pelo que nada tem a opor à realização deste projecto de investigação.

Appendix II: Questionnaire of breast autologous reconstruction

U. PORTO
FEUP FACULDADE DE ENGENHARIA
UNIVERSIDADE DO PORTO

SÃO JOÃO

INFORMAÇÃO AOS VOLUNTÁRIOS

Projeto de investigação: **Estudo da Caracterização térmica dos retalhos utilizados em cirurgia plástica e reconstrutiva**

Faculdade de Engenharia da Universidade do Porto
Centro Hospitalar S. João, EPE

1. **O porquê deste projeto de investigação?**

O principal objetivo deste estudo centra-se na caracterização térmica dos retalhos utilizados na reconstrução mamária em pacientes mastectomizadas, através da técnica da termografia infravermelha. A obtenção da caracterização da anatomia vascular referente ao retalho autólogo em estudo permite fornecer informação complementar e essencial para que os médicos cirurgiões possam escolher o retalho de forma mais consistente e acertada no processo cirúrgico.

Que informação nos fornece a imagem termográfica?

A imagem térmica indica a distribuição da temperatura na superfície da pele. De acordo com a escala pré-estabelecida os tons de azuis representam áreas com temperatura inferior enquanto que os tons avermelhados representam zonas com temperatura mais elevada, tal como ilustra a imagem seguinte:

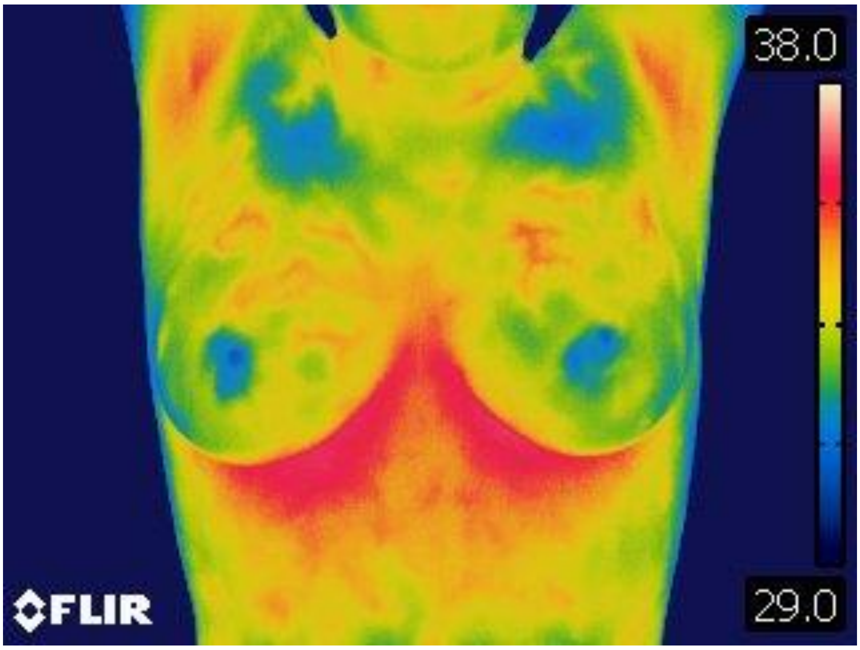


Figura 1: Imagem térmica mamária

A termografia médica é um método complementar de diagnóstico e terapêutica por imagem simples, rápido, não-ionizante, não-invasivo, inofensivo e indolor, portanto livre de riscos para os utentes. As imagens recolhidas vão ser usadas para fins clínicos e académicos, sendo que os dados de cada utente irão ser preservados e mantidos confidenciais, assim como toda a informação irá ser guardada de forma segura.

2. **O que necessito que faça para participar neste projeto?**

É necessário antes da captura das imagens térmicas que a paciente permaneça numa sala aclimatizada expondo a área de interesse por um período de 10 minutos. Enquanto isso, o individuo deverá preencher e tomar conhecimento de alguns formulários. Entre estes incluem-se, o consentimento informado e o questionário.

No dia da recolha algumas precauções deverão ser tomadas antes do período de recolha, tais como:

- Evitar ingerir uma refeição pesada e ingestão de café ou chá até 2h antes;
- Evitar participar em atividades desportivas ou de fisioterapia nas últimas 6 horas anteriores ao exame;
- Não ingerir bebidas alcoólicas e fumar, num período até 2h antes;
- Evitar a ingestão de medicamentos, nomeadamente: esteróides, bloqueadores do sistema nervoso autónomo e medicações vasoactivas, opiáceos e autocolantes dérmicos, pelo menos 24 horas anteriores ao exame.
- Remover todo o tipo de bijuteria presente e evitar o uso de roupas justas e apertadas ao corpo, próximo da área de interesse durante o período de captura;
- Não aplicar qualquer tipo de óleos ou cremes na superfície da pele;
- Por fim, permanecer estático durante 10 minutos, sem cruzar pernas ou braços, ou entrar em contacto entre partes do corpo nas zonas de interesse para o exame.

3. **Quais os benefícios que este estudo apresenta?**

Este estudo permite maior aferição da localização dos vasos perfurantes que poderá diminuir as complicações cirúrgicas. Para além disso, este projeto de investigação contribuirá para uma avaliação objetiva do processo pós-cirúrgico.

4. **Quais os riscos e incómodos que este estudo apresenta?**

Neste estudo não estão contemplados quaisquer riscos ou incómodos para o doente.

5. **Quanto tempo vai durar?**

A participação de cada indivíduo neste projeto irá demorar aproximadamente 20 minutos nas fases pré e pós-operatórias (incluindo o tempo de aclimatização).

6. **Vou ser pago pela minha participação?**

Infelizmente, este projeto não possuí financiamento, pelo que não poderá receber qualquer pagamento pela sua participação neste estudo. Contudo, irá contribuir significativamente para desenvolvimentos únicos e importantes na área da utilização da termografia médica na avaliação da dominância vascular do pulso. Após a participação, as imagens recolhidas poderão também ser enviadas via email caso sejam solicitadas pelo participante.

7. **Contacto**

Nome: Diana Filipa Passos Dias Marques de Abreu
Instituição: Faculdade de Engenharia da Universidade do Porto
email: dianamarques77@hotmail.com

QUESTIONÁRIO

Recolha de imagens termofisiológicas da mama

Voluntário:__________

Dados biométricos:

Idade:		Altura (m):		Peso (Kg):		Menstruação (dias):	

Questionário:

Alguma vez teve cancro da mama? ___________

Se sim, quantas vezes? ___________

Tem histórico familiar desta patologia? ___________

Se sim, quantas pessoas? ___________

Grau de parentesco?___________

Tem ou teve alterações na mama? ___________

Se sim, quais?________________________________

Alguma vez foi submetida a radioterapia na região mamária?_________

A primeira menstruação surgiu antes dos 12 anos?_________

Teve o primeiro filho depois dos 30 anos?_________

A menopausa surgiu depois dos 55 anos?__________

Após menopausa, faz ou fez terapêutica hormonal de substituição durante pelo menos 2 anos?_________

Appendix III: Questionnaire of burn patients

U.PORTO
FEUP FACULDADE DE ENGENHARIA
UNIVERSIDADE DO PORTO

SÃO JOÃO

Serviço de Cirurgia Plástica, Reconstrutiva e Unidade de Queimados

Recolha de Imagens Termográficas de Queimaduras

Voluntário: __________

Dados Biométricos

Idade		**Sexo**		**Altura**		**Peso**		**Menstruação**	

Dados Clínicos

- **Tipo de Queimadura**

Química		**Elétrica**		**Chama**		**Água**		**Outro**	

- **Características da área queimada**

Superficial

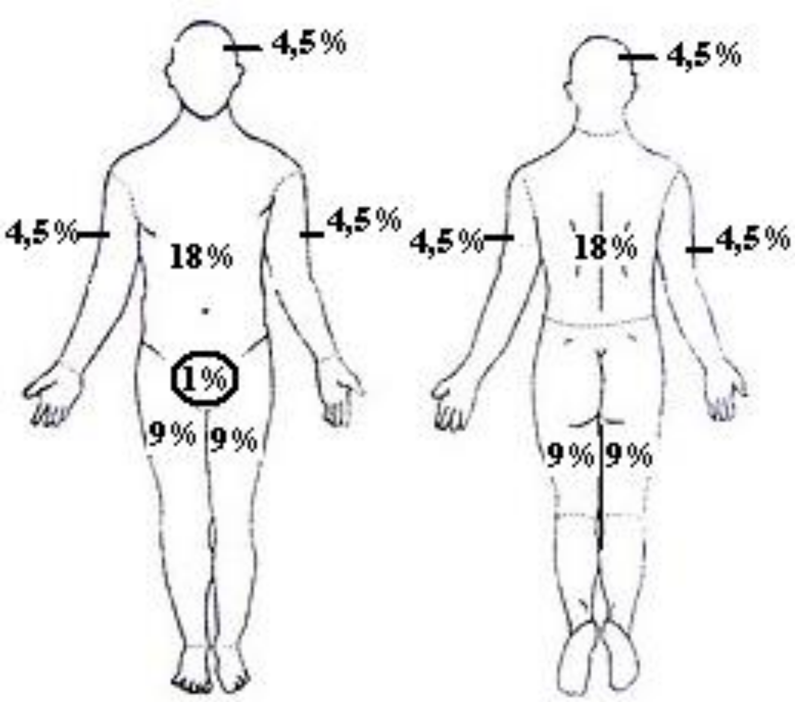
Rosa		**Vermelha**		**Seca sem bolha**	

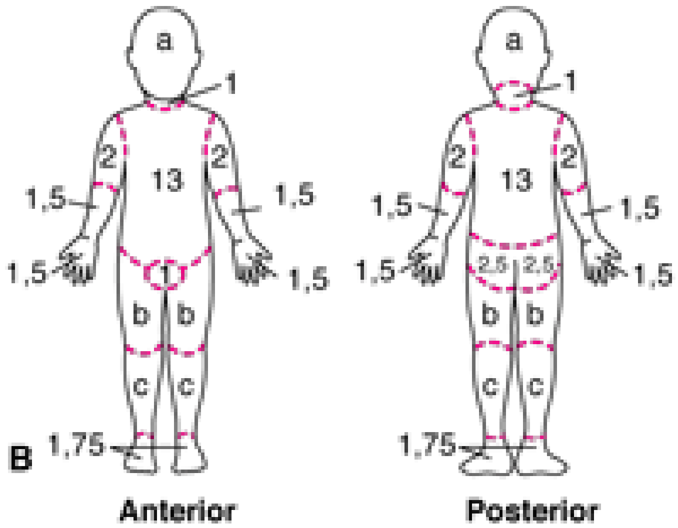
Intermédia Superficial (Preenchimento a cor azul na figura)

Rosa		**Vermelha**		**Dor**		**Humidade**	

Intermédia Profunda / Profunda (Preenchimento a cor vermelha na figura)

Branca		**Vermelho Escuro**		**Carbonizado**		**Dor na periferia**	





	IDADE				
Parte do corpo	0 ano	1 ano	5 anos	10 anos	15 anos
a = 1/2 da cabeça	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2
b = 1/2 de 1 coxa	2 3/4	3 1/4	4	4 1/4	4 1/2
c = 1/2 de 1 perna	2 1/2	2 1/2	2 3/4	3	3 1/4

- **Percentagem total de área queimada**

% Intermédia Superficial		% Intermédia Profunda/Profunda	% Total
	+		

=

- **Observações**

____
____
____
____
____
____

Appendix IV: Thermographic image capture protocol

Protocolo de dados termofisiológicos

Sala de exames

- Deve ser mantida uma distância mínima entre a câmara termográfica e o voluntário – normalmente 1 metro. A sala deve ter, no mínimo, 2x3 metros.
- A sala deve conter apenas o material necessário para a recolha de imagens, de forma a evitar reflexões térmicas e criar artefactos nas imagens.

Ambiente controlado

- A sala deve ser mantida a uma temperatura constante entre 18-24°C, normalmente 22±1°C, e será necessário que antes de iniciar a captura das imagens, que o voluntário permaneça na sala durante 10 minutos para que o seu corpo se mantenha em equilíbrio com a temperatura da sala.
- Radiação ultravioleta deve ser evitada. Todas as janelas e portas devem ser devidamente fechadas.
- A humidade relativa deve ser inferior a 50%.
- A sala deve conter um equipamento de ar condicionado, de forma a manter a temperatura recomendada constante. O fluxo de ar proveniente do equipamento não deve ser orientado para o paciente.
- O equipamento deve ser mantido fora da zona do voluntário, de modo a evitar perturbações.
- Deve existir um cubículo mínimo na sala de exame, com as mesmas condições ambientais, para que o voluntário possa retirar/vestir as roupas com privacidade e descansar durante o período de aclimatização.
- Não deve haver luz diretamente incidida no voluntário, para evitar reflexões térmicas.

Cuidados para o equipamento termográfico

- A câmara termográfica deve ser ligada 20 minutos antes da captura de imagens.
- O equipamento deve garantir um foco automático ou manual.
- É recomendado o uso da temperatura externa como referência para a calibração, de modo a garantir a qualidade da imagem e sensibilidade da câmara.
- O tipo de lentes da câmara deve ser considerado. Lentes com ângulos mais abertos reduzem a distância entre a câmara e o sujeito, mas ao mesmo tempo aumentam a distorção periférica da imagem.
- Cada imagem, ou conjunto de imagens deve indicar a gama de temperatura usada e o respectivo código de cor/ escala de temperaturas. A escala e gama de cores, comummente utilizado em aplicações médicas, varia entre 27°C e 37°C.
- As temperaturas do fundo que podem diminuir a intensidade da imagem devem ser evitadas. As respectivas cores devem ser substituídas por branco, preto ou cinzento, de forma a conseguir uma melhor apresentação visual.

Informação para o voluntário

O voluntário deve ser informado para:

- Evitar o uso de aplicações tópicas: como o uso de ornamentos (joalharia) e maquilhagem no dia do exame.
- Evitar grandes refeições e ingestão de café ou chá duas horas antes do exame.
- Não fumar durante duas horas antes do exame.
- Evitar o uso de roupas muito justas e apertadas.
- Evitar a prática de exercício físico incluindo métodos de fisioterapia, como: electroterapia, ultrassons, tratamento com calor, crioterapia, massagens e hidroterapia, nas últimas 6 horas antes do exame.
- Evitar a ingestão de medicamentos, nomeadamente: esteroides, bloqueadores do sistema nervoso autónomo e medicações vasoativas, opiáceos e autocolantes dérmicos, pelo menos 24 horas antes do exame. Exceções devem ser anotadas.

Preparação pré-recolha

- O voluntário deve ser informado sobre os procedimentos do exame, antes do seu início.
- O voluntário deve ser instruído para retirar a roupa e os ornamentos (joalharia) que tiver na face.
- O voluntário deve ser informado para sentar-se ou descansar na sala de exames no período de aclimatização. O período mínimo é de 10 minutos.
- O voluntário deve evitar contacto com a face.

Posições para a recolha das imagens

- O voluntário deve assumir posições corretas, de forma a serem adquiridas vistas padrão da face.
- Alguma comparação/conclusão obtida em diferentes condições deve ser evitada.

Campo de visão

- O voluntário deve conservar a distância mínima à câmara estabelecida, para que o campo de visão varie o mínimo possível. O tamanho da imagem está dependente desta distância e da distância focal da lente da câmara.