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Footnotes

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Abstract

Breast cancer is the most frequent cancer among women and is responsible for the highest number of cancer-related deaths. Approximately 40% of the patients with breast cancer will undergo a mastectomy. Breast amputation is a lifesaving but mutilating procedure. Therefore a good quality of life and a good cosmetic outcome is mandatory after breast cancer treatment. Reconstructive breast surgery aims to recreate a natural looking breast that is warm, soft and feels natural. The chosen reconstruction technique depends on the physiognomy of the patient, technical skills of the surgeon and most important the expectations of the patient. The idea of 'like-by-like' replacement refers to reconstruction of a natural-looking, warm, soft and ptotic breast that matches the contralateral side. Autologous breast-reconstruction matches these expectations. Autologous breast reconstructions with free flaps evolved from prolonged and laborious procedures with only limited free flaps available, to routine surgeries with a widespread availability of flaps to use. The first publication of free tissue transfer for breast reconstruction was in 1976 by Fujino. Two years later Holmström was the first to use the abdominal pannus for breast reconstruction. Over the next four decades multiple free flaps have been described. The possible options for donor site are the abdomen, the gluteal region, the thigh and the lower back. During this evolution the reduction of donor site morbidity became more important. Present article gives an overview of the evolution of free tissue transfer in breast reconstruction, highlighting the most important milestones.AQ2

KEYWORDS

Perforator flaps; breast reconstruction; history; plastic surgery; breast cancer

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None.

Introduction

Background: Breast cancer is the most common cancer in women worldwide [1]. In 2018, there were over 2 million cases. Belgium is the country with the highest rate of breast cancer in the world (113/100.000). The five years survival in Belgium is 83%, which is equal to the average five year survival for breast cancer in Europe (82%) [2]. The keystones in breast cancer treatment are patient's survival and minimizing treatment's morbidity. Approximately 40% of the patients with breast cancer undergoes a mastectomy. Breast amputation is a lifesaving but mutilating procedure. Therefore a good quality of life and a good cosmetic outcome is mandatory after cancer surgery [3]. Reconstructive breast surgery aims to recreate a natural looking breast that is warm to touch [4]. The chosen technique, either implant-based or autologous breast reconstruction, depends on the physiognomy of the patient, technical skills of the surgical team and most important the expectations of the patient. Results: The idea of 'like-by-like' replacement refers to reconstruction of a natural-looking, warm, soft and ptotic breast that matches the contralateral side. Autologous breast reconstruction matches these expectations. Arestide Verneuil (1823–1895) was the first to describe the use of autologous tissue to reconstruct the breast. He devoted the first of the 6 volumes of his 'Mémoires de Chirurgie' to 'Chirurgie réparatrice', and cites the case of a 50 year old female patient, he operated upon in the Hôtel-Dieu hospital in Paris in 1858, after she had four previous resection for breast cancer. Verneuil reconstructed the defect with breast tissue from one side transferred on a pedicle to the opposite side. The patient survived but ultimately died from cancer recurrence [5,6]. Vincent Czerny (1842–1916), a German surgeon, was credited with the first successful autologous breast reconstruction after mastectomy. He described an autotransplantation of a lipoma from the patient's lumbar region to the mastectomy side [6,7]. This success generated a search for multiple autologous methods to reconstruct the breast. Pedicled locoregional flaps such as the musculocutaneous latissimus dorsi (LD)-flap and the transverse rectus abdominis myocutaneous (TRAM)-flap were the workhorse flaps for years [8]. Evolution in microsurgery now allows transplantation of large volumes of autologous tissue from an anatomically remote area [9]. Over the last four decades a tremendous evolution has been seen in this part of reconstructive surgery. Autologous breast reconstructions with free flaps evolved from prolonged and laborious procedures with only limited flaps available, to routine surgeries with a widespread availability of potential flaps to use.

Conclusion: While implant-based breast reconstruction is an important and frequently used technique, this article aims to present an overview of the evolution of free tissue transfer in breast reconstruction, highlighting the most important milestones.

A new era

In 1976, Fujino published the first case report of a free tissue transfer to reconstruct a breast after radical mastectomy. A skin-fat-muscle flap from the upper portion of the greater gluteal muscle was harvested including the superior gluteal artery and vein. A successful microvascular anastomosis was performed connecting the superior gluteal vessels to the thoracoacromial artery and lateral thoracic vein. The same authors reported the use of a gluteal free flap for the reconstruction of a congenital aplastic breast [10,11]. In 1978, Serafin et al. were the first to describe a series of free flaps to reconstruct the breast after radical mastectomy. Ten groin flaps and two contralateral LD-flaps were used in combination with an implant in twelve patients [12]. Holmström was the first to use the abdominal pannus as donor site to reconstruct the breast. This flap was called the free abdominoplasty flap, which was based on the inferior epigastric vessels and a superficial vein [13]. Basically Holmstöm was the first to describe and perform a free TRAM flap.

Abdominal flaps

Holmström's work drew attention to the availability of the abdominal donor site for microsurgical breast reconstruction. However, the idea to use the excess of abdominal fat was not new. In 1943, Sir H. Gillies already performed breast reconstructions by tubing the excess of abdominal fat to the trunk over several stages [14]. In 1979, the first pedicled rectus abdominis myocutaneous flap was reported by Robbins with a vertically designed skin island. This design resulted in inappropriate scarring on the abdomen [15]. The use of the abdominal tissue for breast reconstruction was not popularized until 1982, when Hartrampf published his work on the pedicled 'transverse abdominal island flap'. Clinical observations during abdominoplasty procedures revealed that the abdominal pannus remains vascularized and can be islanded when it is only attached to the anterior rectus sheath. This clinical research revealed that a musculocutaneous flap can be elevated on the deep superior epigastric vessels. Three designs of this musculocutaneous flap were described; the vertical-, the horizontal upper- and the horizontal lower rectus abdominis musculocutaneous flap. The latter is known as the pedicled TRAM flap. Reported advantages were well vascularized tissue, large arc of rotation and usage of abdominal fat obviating the use of an additional implant, resulting in a durable and natural appearing breast [16]. Despite the excellent results with pedicled TRAM flaps, important shortcomings were encountered. The risk of abdominal hernia was already described in the first report by Hartrampf. Vascular complications on the other hand were reported by Scheflan and Dinner in their own described zones III and IV, which we peculiarly known as the Hartrampf perfusion zones of the abdominal flap. Strict patient selection was essential to avoid vascular complications [17]. The potential vascular complications are accountable to the dominance of the deep inferior epigastric artery in supplying the skin of the anterior abdominal wall, as proven by Boyd in 1984 [18]. A free abdominal flap, requiring microvascular transfer, based on the inferior epigastric pedicle was growing popular in the mid to late 1980s to overcome the vascular problems. Friedman was the second, after Holmström in 1979, to report a case of a free TRAM flap in 1985 with excellent results [19]. The teams of Arnez and Grotting improved the operative technique and surgical outcome. The free TRAM flap has a superior perfusion compared to the pedicled TRAM flap by using the dominant vascular supply. On top of a better vascularization the free TRAM flap gives an improved medial contour, maintains the inframammary fold due to the lack of tunneling the rectus muscle and lastly a TRAM flap needs a more limited rectus muscle harvest. The length and size of the pedicle allows for feasible microvascular anastomosis. Recipient vessels were branches of the axillary vessels in all cases. The free TRAM flap was favorable concerning complications, operating time, estimated blood loss, hospitalization, and return to functional baseline [20,21].

The introduction of perforator flaps, composed exclusively of skin and subcutaneous tissue, represented a significant advance in microsurgical reconstructions. The first publication in 1988 on this new type of flap described the reconstruction of low posterior midline defects with perforator flaps [22]. Koshima and Soeda were the first to describe a perforator flap of the anterior abdominal tissue in 1989. They described an inferior epigastric artery skin flap without rectus abdominis muscle to reconstruct a groin defect as a pedicled island flap and to reconstruct the oral floor as a free flap. This large flap without muscle could survive on a single muscle perforator [23]. Advantages of perforator flaps are reduced donor-site morbidity, longer pedicles compared to musculocutaneous flaps and more freedom in orientation of the pedicle [24]. Allen and Treece developed in 1994 the deep inferior epigastric artery perforator flap (DIEP) for breast reconstruction after mastectomy. The technique has all of the advantages of the free TRAM flap with decreased risk for abdominal weakness, bulging or hernia due to complete muscle preservation [25]. Blondeel published in the same year his refinements to the technique. He performed the first bipedicled DIEP flap for single breast reconstruction, using the internal mammary artery as recipient vessel [26]. In 1997, Blondeel confirmed the superiority of DIEP flaps compared to free TRAM flaps in donor site morbidity. The long term benefits for the patient outweigh the increased surgical complexity, operating times and cost involved in DIEP flap breast reconstruction [27]. In 1991, Grotting was the first to perform a breast reconstruction with abdominal tissue based on the superficial epigastric artery and vein with complete sparing of the rectus abdominis muscle and fascia [28]. More experience with this flap was presented by Arnez in 1999. The advantages of this flap are the fast and easy dissection and absence of any potential muscular disturbance. However there are some major drawbacks related to this technique: size and length of the pedicle is considerably less compared to DIEP flap, unfavorable pedicle orientation arising from the flap border, unreliable perfusion across the midline and inconsistent anatomy of this vessels [29]. In 1994, a breast reconstruction with a free musculocutaneous flap based on the deep circumflex iliac artery of the lateral abdomen was described by Hartrampf [30]. The so called Rubens flap can be used when the abdominal pannus is not available [31]. Later it was refined as a perforator flap and it's first use in breast reconstruction was described by Buchel [32].

Over the years, the DIEP flap has become the gold standard for autologous breast reconstruction and different pioneers of the DIEP flap have published their experience with this technique [33–36]. In 2002, Nahabedian added the concept of a muscle sparing (MS)TRAM-flap, depending on the amount of rectus muscle that is preserved [36] (Table 1).

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Table 1. History of the abdominal pannus as donor site in breast reconstruction.

1979 Report of the first abdominal free flap for breast reconstruction 'free abdominoplasty flap', later known as the free TRAM flap – Holmström et al. [13]

1979 Description of the first pedicled rectus abdominis myocutaneous flap with vertical designed skin island – Robbins et al. [15]

1982 Description of the pedicled TRAM flap – Hartrampf et al. [16]

1991 First abdominal free flap based on the superficial epigastric vessels for breast reconstruction, later known as the SIEA flap – Grotting et al. [28]

1994 Description of the DIEP flap in breast reconstruction – Allen et al. [25]

1994 First bilateral DIEP flap breast reconstruction – Blondeel et al. [26]

Abbreviations: TRAM: transverse rectus abdominis myocutaneous; SIEA: superficial inferior epigastric artery; DIEP: deep inferior epigastric perforator.

In general, the abdominal donor site was already established in breast reconstruction for its volume, color and texture resemblance with native breast tissue and for its potency to match a ptotic opposite breast that tends to age in a natural fashion. Therefore attention shifted to decreasing donor site morbidity. This was seen over the years by altering techniques from pedicled to free TRAM flap, to free MS-TRAM flap, DIEP flap and SIEA flap. Progress comes at a price however.

Detection of perforator location

Due to the increased complexity of perforator flaps such as the DIEP flap, a higher risk for (partial) flap failure, venous congestion and fat necrosis is observed [37,38]. Selection of the best perforator vessels is the key in perforator flap surgery. This will reduce operative time, lower complication rates and ensure an overall better result [39]. Current techniques to locate the perforator vessels include handheld Doppler, color Doppler ultrasound (CDU), Magnetic Resonance Angiography (MRA), computer tomographic angiography (CTA) and dynamic infrared thermography (DIRT) [40–43]. Table 2 compares the different techniques. The current gold standard to map the perforators is CTA on which the location and hemodynamic properties of the flap can be assessed [40–42]. CTA replaced CDU over the years. CDU is a safe and cheap technique that gives information on the diameter and blood flow characteristics of the perforator vessels, but is has a high inter-observer variability and a high number of false positives compared to CTA [40,41,44–47]. Moreover it is a time consuming examination. CTA is frequently used because it is non-invasive and has a high spatial resolution with visualization of the intramuscular course of the vessels. However, this technique has disadvantages, such as the use of intravenous (IV) contrast agents and ionizing radiation, high purchasing costs, a lack of perioperative usability, and a lack of physiological information on flow characteristics [40]. DIRT has gained in popularity as an alternative technique in perforator mapping [42]. DIRT is less invasive than CTA because it does not use radiation nor contrast agents. It is based on measurements of heat emission by tissues and skin temperature with the use of infrared (IR)-cameras. Data obtained with DIRT are used to generate color-coded maps that correlate with the perfusion of the skin. DIRT is generally used as a dynamic investigation technique, meaning that the skin must undergo a thermal cold challenge. After this cold challenge, DIRT measures the rate and patterns of rewarming. With this method, clinicians are able to identify the most dominant perforators and their perfusion area [43,48]. Earlier studies have shown that DIRT is a valuable addition during breast reconstructions with DIEP flaps pre, per-, and post-operatively [45,46,48–53]. DIRT is a valuable alternative to clinical examination to evaluate at any stage during surgery the

perfusion of the flap [42]. DIRT can also be an interesting alternative to the use of indocyanine green (ICG) to evaluate the microcirculation and perfusion of the flap peroperatively. DIRT is less invasive than the use of ICG because there is no need for contrast agents. Moreover the potential allergic reactions to ICG should be taken into consideration [54]. Furthermore, DIRT is easy to interpret and has a low purchasing cost. DIRT only provides information on the physiology of the perforator and not on the morphology [43]. Nevertheless, adding DIRT during breast reconstructions with DIEP flaps is a helpful tool [42,43,46]. This opens also possibilities for its use in other free flaps.

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Table 2. Comparison of various tools for assessing characteristics of the perforators.

	CDU	CTA	DIRT
Cost	Cheap	Expensive	Cheap
Radiation and contrast	No	Yes	No
Easy to perform and interpret by surgeon	No	No	Yes
Operator dependent	Yes	No	No
Time consuming	Yes	Yes	No
Applicable in all phases of DIEP (pre-, per- and postoperative)	No	No	Yes
Information on flow (physiology)	Yes	No	Yes
Information on perfusion	No	No	Yes
3D images	No	Yes	No
Precise anatomical description (morphology)	No	Yes	No

Abbreviations: CDU: color Doppler ultrasound; CTA: computed tomography angiography; DIRT: dynamic infrared thermography.

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Table 3. History of the gluteal and lower back as donor sites in breast reconstruction.AQ5

1976 The first report of free tissue transfer to reconstruct the postmastectomy defect was with a superior gluteal myocutaneous free flap – Fujino et al. [11]

1989 Description of the inferior gluteal myocutaneous free flap in breast reconstruction – Paletta et al. [58]

1995 Description of the SGAP flap in breast reconstruction – Allen et al. [59]

2003 Report of the LAP flap to reconstruct the breast – de Weerd et al. [75]

2004 Description of the IGAP flap in breast reconstruction – Guerra et al. [60]

2007 First report of the FCI flap in breast reconstruction – Papp et al. [62]

Abbreviations: SGAP: superior gluteal artery perforator; LAP: lumbar artery perforator; IGAP: inferior gluteal artery perforator; FCI: fasciocutaneous infragluteal.

The abdominal donor site is not always available, for example in cases of insufficient soft-tissue bulk, history of abdominoplasty, or multiple abdominal scars. With increasing numbers of patients requesting autologous reconstructions other donor sites are considered [55].

Gluteal flaps

After the initial report of Fujino 1976, using a superior gluteal myocutaneous free flap, Le-Quang performed the first breast reconstruction with an inferior gluteal myocutaneous free flap in 1978 [11,56]. Table 3 Shaw popularized breast reconstructions by means of the superior gluteal myocutaneous free flap, with excellent results and minor donor site morbidity. However, due to inherent short vascular pedicle, a venous graft was often necessary, consequently constraining its use [57]. The inferior gluteal myocutaneous free flap was further elaborated by Paletta in 1989. Despite increased length of the vascular pedicle and a more discrete scar compared to the superior gluteal flap, the inferior gluteal flap never grew as popular because of the close relation to the sciatic nerve with potential injury and more pain when sitting [58]. In 1995, Allen published a microsurgical breast reconstruction using a free gluteal perforator flap with longer vascular pedicle and without sacrificing the muscle: the superior gluteal artery perforator (SGAP) flap [59]. In 2004, the same team published their experience with 142 gluteal artery perforator flaps, including 6 cases of an inferior gluteal artery perforator (IGAP) flap, which was until then not yet reported for breast reconstruction. The IGAP flap was abandoned early in their series due to the morbidity related to the sciatic nerve. The donor site scar of the SGAP flap is well hidden, but an important disadvantage is contour deformity of the buttocks, especially in oblique oriented designs [60]. In general, redundant gluteal adiposity in a patient, made the SGAP the first choice flap for many years when the abdominal donor site was not available. Nevertheless, the gluteal flaps have several shortcomings: They are challenging to dissect, have a short vascular pedicle, are more difficult to shape since the gluteal fat tends to be more rigid and the scar can result in a contour distortion of the buttocks [61]. In 2007, Papp published the first report of an alternative free flap of the inferior gluteal region based on the descending branch of the inferior gluteal artery that accompanies the posterior femoral cutaneous nerve and emerges from under the edge of the gluteus maximus muscle. This flap, which is called the fasciocutaneous infragluteal (FCI) flap, can easily be harvested as an neurovascular flap by adding branches of the posterior femoral cutaneous nerve and has a long pedicle of up to 18 cm. However, sensory changes to the donor site were present in 68% of patients [62]. Because of the

abovementioned shortcomings related to gluteal flaps microsurgeons started exploring other donor sites.

Thigh flaps

Medial thigh

Yousif et al. were the first to describe the medial thigh as donor site for breast reconstruction using a free musculocutaneous gracilis flap with transverse-oriented skin island in 1992. They discovered during cadaver dissections that perforators from the gracilis pedicle had a tendency to travel in a transverse direction, resulting in a transverse clinical territory in the upper inner thigh. They described a single case of breast reconstruction with this free flap. For the microvascular anastomosis to the axillary artery and vein a vein graft was used [63]. The use of this transverse myocutaneous gracilis (TMG) or transverse upper gracilis (TUG) flap in reconstructive breast surgery was further refined by Wechselberger and Schoeller in 2004 and 2011. It is considered a valuable alternative for breast reconstruction after skin-sparing mastectomy in patients with small to moderate sized breasts and unavailable abdominal tissue. Flap harvest is fast and easy, since this is not a perforator flap. Reported donor site morbidity was minimal and is similar to a classical medial thigh lift [64,65]. Donor site complications of 60% are reported, mostly sensory disturbances and wound dehiscence. Aggressive tissue harvest can lead to lymphedema and labial spreading. Conservative tissue harvest is paramount to avoid these complications and flap width should not exceed 8 cm [66,67]. Modifying the design of the skin island avoids many donor site complications. Despite the known perfusion related complications of the distal third of the skin along the axis of the gracilis muscle, Park et al. renewed the interest for using a vertical designed skin island, known as the vertical upper gracilis (VUG) flap. They also describe the possibility to use bilateral stacked flaps (BUG) for reconstruction of larger breasts [68]. Dayan described in 2013 the diagonal upper gracilis flap (DUG), a modification of the TUG flap whereby the skin island is oriented along the line of least tension (Langer's lines). Compared to the VUG flap, the distal third is more reliable since it is closer to the clinical territory of the gracilis pedicle [69].

Posterior thigh

The use of the posterior thigh as donor site for autologous breast reconstruction was introduced in 2012 by Allen et al. They were the first to use the profunda artery perforator (PAP) flap for breast reconstruction. This flap is the perforator version of the posterior thigh myocutaneous flap used to reconstruct pressure sores. It is based on a perforator of the deep femoral vessels (profunda femoris artery and vein) coursing through the adductor magnus muscle. Advantages compared to the TUG/TMG flap are a longer pedicle, sparing the muscles and orienting the skin island away from the lymph nodes in the femoral triangle. Disadvantages are related to the transverse orientation of the flap [70].

Lateral thigh

Already in 1990, Elliott used the lateral transverse thigh free flap as an alternative flap for autologous breast reconstruction in women with excess of fat in the upper lateral thigh or saddlebag deformity [71]. It was later refined to a perforator flap in 2011 by Kind [72]. Hereafter, the flap was

further elaborated by Tuinder and renamed septocutaneous tensor fascia latae (sc-TFL) flap or lateral thigh perforator (LTP) flap. Due to excellent results this flap is second choice after the DIEP flap in their department [73]. Also the anterolateral thigh (ALT) flap, a workhorse flap in soft tissue reconstruction, was applied for reconstruction of the post mastectomy defect and first described by Wei [74]. But because of conspicuous scarring and limited bulk it was never popularized for this indication (Table 4).

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Table 4. History of the thigh as donor site in breast reconstruction.

1990 First communication of the lateral transverse thigh free flap for autologous breast reconstruction – Elliott et al. [71]

1992 First report of the medial thigh as donor site in breast reconstruction by free musculocutaneous gracilis flap – Yousif et al. [63]

2004 Popularization of TMG/TUG flap in breast reconstruction – Wechselberger et al. [64]

2012 Description of PAP flap in breast reconstruction – Allen et al. [70]

2013 Description of a diagonal oriented gracilis free flap or DUG flap – Dayan et al. [69]

2018 Description the sc-TFL or LTP flap in breast reconstruction – Tuinder et al. [73]

Abbreviations: TMG: transverse myocutaneous gracilis; TUG: transverse upper gracilis; PAP: profunda artery perforator; DUG: diagonal upper gracilis; sc-TFL: septocutaneous tensor fascia latae; LTP: lateral thigh perforator.

Lower back

The newest donor site in the armamentarium of the reconstructive breast microsurgeon is the lower back. In 2003, de Weerd was the first to present breast reconstruction with a lumbar artery perforator (LAP)-flap [75]. Refinements of the technique were made and published by Opsomer. The most important advantages are the texture of the lumbar fat, which is softer compared to gluteal fat making the shaping much easier, and the minimal contour defect despite of large harvested flaps. The major downside with this flap is the very short pedicle which routinely requires interposition grafts. In Ghent, the LAP flap turned into the favorite second-choice flap for autologous breast reconstruction [76].

Future of breast reconstructions

There has been a tremendous and successful progress in reducing donor site morbidity in breast reconstructions with free flaps over the past decades. We believe the esthetic outcome of breast

reconstructions will further improve and the donor site morbidity will further diminish in the next years. Tissue regeneration is actively researched to create autologous, tissue engineered, 3D composite tissues. The creation of these tissues could open a whole new era of tissue transplantation without donor site morbidity.

Conclusion

Women confronted with mastectomy after breast cancer have many options when considering an autologous breast reconstruction. A multidisciplinary surgical approach resulted in in an exponential growth in breast reconstruction possibilities. A reconstructed breast should appear and feel realistic using reconstructive surgery with minimal donor site morbidity and low-risk surgery. Microsurgical breast reconstruction with perforator flaps offers reliable, durable and esthetically pleasing reconstructions, with minimal functional donor site morbidity. The abdominal donor site with the DIEP flap remains the workhorse for the reconstructive microsurgeons, offering a reliable flap with a good donor site morbidity and pleasing esthetical outcome. Careful patient selection, surgical planning and technical execution are essential to success of the surgical treatment. When the abdomen is not available the thigh flaps (TMG/TUG/PAP) are useful as a second choice. The flaps from gluteal region can be used as a lifeboat. The use of CT scan helps the microvascular surgeon to select the perforator with best vascularization. DIRT is a novel technique which has to potential to contribute to minimize complications and improve outcomes in the future.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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