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Review

Alternative imaging technologies for perforator mapping in free flap breast reconstructive surgery - A comprehensive overview of the current literature

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Summary *Background:* The use of perforator mapping has become routine for many microsurgeons in the planning and performing of free flaps in breast reconstructions. Within this field, the number of available technologies and their quality has rapidly evolved over time. This study presents an up-to-date review on the spectrum of alternative perforator mapping modalities and the efficiency and utilization in the practice of free flap breast reconstructive surgery.
Methods: Extensive searches of the PubMed and Embase databases were performed. Articles containing free flap tissue transfer in breast reconstruction and a perforator imaging modality were included. Qualitative and descriptive analyses of the outcomes were performed, and the quality of the evidence was appraised.
Results: One hundred and sixty-eight articles were included. Besides the routinely used handheld Doppler, CT angiography, and MR angiography, seven alternative technologies (38 studies) have been found; color Doppler fluorescent angiography, dynamic infrared thermography, image-guided stereotaxy, template, 3D printed model, and augmented reality. The modalities were classified based on their concept of imaging as *volumetric perforator imaging, real-time*

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perforator imaging, and *complementary techniques*. A poor level of evidence for each alternative modality was found.

Conclusion: An overview of alternative imaging techniques available to pre- and intraoperatively map perforator locations have been given. Several novel promising techniques have been identified, all to be used in conjunction with volumetric imaging. This overview provides a perspective on the future field of imaging in reconstructive surgery.

Contents

Introduction

The high incidence of breast cancer and the growing number of breast cancer patients opting for mastectomy over breast-conserving operations have led to breast reconstruction becoming an important part of breast cancer management.[1] Besides implants, free flap autologous breast reconstruction is a valuable option as it, due to its natural feeling and appearing breast, is durable and can mature with the patient over time, while avoiding the potential for implant-related complications.[2-5]

During the procedure of free flap surgery, the dissection of the supplying blood vessels is a crucial step. It consists of localizing the dominant perforator and dissecting its intramuscular course with sufficient pedicle length, while sparing muscle function and minimizing donor site morbidity. The ideal vascular pedicle includes a large-caliber pedicle and perforator (both artery and veins). The perforator has a central location within the flap, a short intramuscular course and it has perforating veins which communicate with the superficial venous network. Broad subcutaneous branching, , longer subfascial course and avoiding tendinous intersections would be convient.[6]

Anatomical studies in the laboratory have created a foundation of knowledge on predictable location and vascular territories of dominant perforators.[7-9] These perforasomes improve our understanding of flap design and safe flap harvest, but there is a high degree of inter- and intravariability among patients.[10,11]

A presurgical vascular map highlights anatomical variance to assist the surgeon in choosing the appropriate perforator. Perforator mapping, predominantly via computed tomography angiography (CTA) or magnetic resonance angiography (MRA), has proven its advantage and is currently widely considered as the standard preoperatively and, in many clinics, adopted in the planning.[12]

However, imaging technology is ever improving, and a large number of techniques have become available. A comprehensive overview of all imaging techniques available to facilitate perforator mapping and selection for breast reconstructive procedures was created. Volumetric perforator imaging (CTA, MRA) and handheld Doppler (HHD) had already been extensively studied and are, therefore, beyond the scope of this comprehensive article.[13-16] The aim of this review is to identify alternative perforator imaging modalities and report on utilization, application, benefits, and limitations to optimize preparation and, consequentially, surgical outcome in microsurgical breast reconstruction.

Method

A literature review was undertaken, using PubMed and Embase databases. For transparency and reproducibility, a full electronic search strategy for both databases has been added, see Appendix. These searches provided a vast number of results, 1156 in PubMed and 1198 in Embase on October 04, 2020, sacrificing specificity for sensitivity.

This review is registered on the PROSPERO database (CRD42019128357); it was designed and conducted in accordance with the Cochrane Handbook of Systematic Reviews and has been authored in accordance with the PRISMA guidelines.

Study selection criteria

Articles linking free flap tissue transfer in breast reconstruction with all perforator imaging modalities, including CTA, MRA, and HHD, were considered for inclusion to capture all studies in this specific field.

After the results were returned, duplicates were deleted, and the full texts were obtained in Endnote X8 (Clarivate Analytics, Philadelphia, USA) (Figure 1). Studies in English in the date range 2004 until 2020 were included (excluding outdated imaging due to the fast evolution of imaging quality). Two independent authors (LS and KP) assessed all studies on Title/Abstract. The inclusion lists were compared, and in case of discrepancies, the final consensus was reached after deliberation of both reviewers. The remaining articles were assessed for inclusion based on the full texts. Articles not describing perforator mapping or the imaging characteristics were excluded. Also, no full text, non-English, cadaver, or animal studies were excluded.

The reference lists of all remaining articles were screened for potentially relevant papers. Again, in case of discrepancies, a final consensus was reached after deliberation of both reviewers or the senior author was consulted.

Data extraction

Both reviewers retrieved data on technology details, imaging method, its use pre-, intra-, and postoperatively, conveniences, and drawbacks. Furthermore, data on number of participants, quality and accuracy of perforator mapping, and the complications rates were extracted.

Assessment of bias

These studies were assessed, independently by both reviewers, for gross errors of construction and subsequently attributed a CEBM evidence level.[17]

Analysis

No meta-analysis could have been performed due to the insufficient number of articles per technology and heterogeneous intervention protocols and outcome measurements. Instead, qualitative and descriptive analyses of the outcomes were given.

Results

Study selection

Titles and abstracts of 1338 unique articles were screened. After screening the full text of 304 articles, 159 were selected for data extraction by two authors (K.P. and L.S.). Nine additional relevant studies were found by screening related articles and citations, resulting in a total of 168 articles (Fig. 1). The majority of articles concerned computed tomography (CT) ($n = 79$), magnetic resonance (MR) ($n = 24$), HHD ($n = 5$), or a combination of these ($n = 16$).

Seven alternative technologies were found in the minority of articles ($n = 38$ studies); color Doppler (Duplex), fluorescent angiography (FA), dynamic infrared thermography (DIRT), image-guided stereotactic navigational systems (image-guided stereotaxy), template, 3D printed model, and augmented reality (AR). Six reviews partly concerning these not routinely used technologies were found. None of those reviews included a meta-analysis. The level of evidence (CEBM) assignable to each technique, the number of articles, and the patients concerned can be found in Table 1.

The modalities were classified based on their concept of imaging as *volumetric perforator imaging* (CTA, MRA), *real-time perforator imaging* (HHD, color Doppler, FA, and DIRT), or *complementary techniques* (image-guided stereotaxy, template, 3D printed model, and AR).

Real-time perforator imaging

Color Doppler (Duplex)

Color Doppler is the presentation of Doppler data with the addition of two-dimensional color to indicate the direction of blood flow.[18] Similar to HHD, this technique is non-invasive but requires an experienced operator (e.g., radiol-

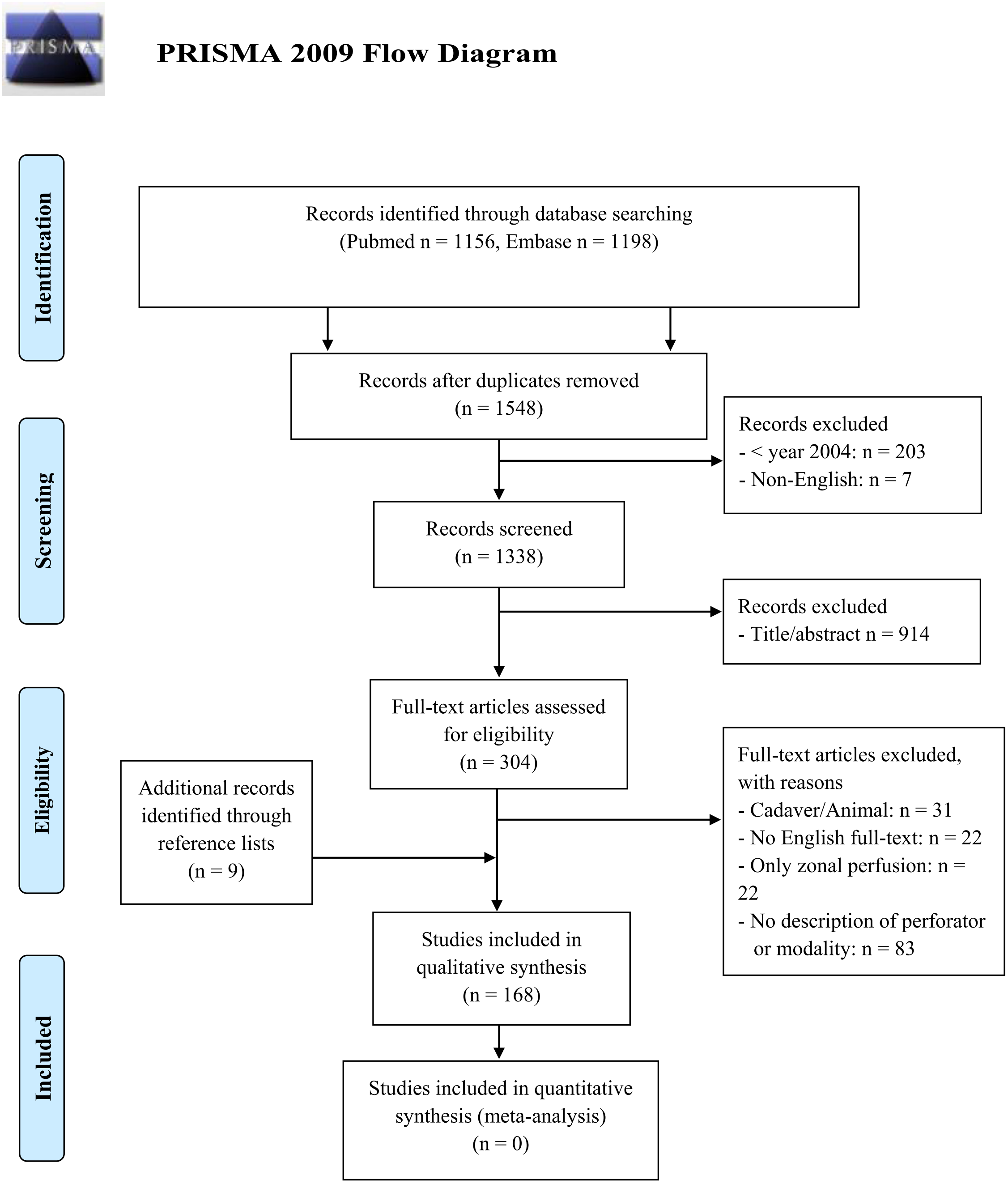

FIGURE 1 Flow diagram of study selection.

Table 1 Number of articles, number of patients, and level of evidence for perforator imaging techniques in plastic surgery, center of evidence-based medicine (CEBM).

Imaging technique	Number of articles	Numberof patients	Level of evidence
Color Doppler (Duplex)	7 (1 RCT)	380	4
Fluorescent angiography	3	36	4
Dynamic infrared thermography	10	105	4
Image-guided stereotaxy	2	5	4
Template	5	63	4
3D printed anatomical model	6	70	5
Augmented reality - wearable	2	6	4
Augmented reality - projector based	3 (1 RCT)	72	3

ogist) and is less portable. Color Doppler has a higher sensitivity and specificity compared to HHD, but it is subjected to a high interobserver variability and was thought to be less accurate than CTA.[19,20] In a prospective cohort, Scott et al. located 63% of the perforators with color Doppler and 100% with CTA.[21] In contrast with the most of literature, Mijuskovic et al. recently published superior results for color Doppler compared to CTA.[22] The number of perforators and perforators larger than 1 mm was significantly higher with color Doppler than with CTA. There was no significant correlation between the intraoperatively chosen perforator and the dominant perforator in the CTA, whereas the correlation between the chosen perforator and the dominant perforators in the color Doppler was significant.

Lindsey et al. published a practical evolution concerning color Doppler.[23] They managed to image perforator flaps with an ultrasound modality which has been downsized to a highly portable, tablet-based color Doppler system. This demonstrates the potential utility of existing modalities when adding new technology.

In the preoperative workflow, all vessels of the abdomen should be screened for finding a suitable perforator, while the same anatomy has to be visualized and marked again perioperatively. This makes color Doppler time-consuming, and care should be taken when imaging repeatedly as color Doppler is highly observer dependent as mentioned before.

Fluorescence near-infrared angiography (FA)

FA is a real-time imaging modality, using an intravenously injected contrast dye. The dye is excited by an external light source that emits radiation at a different wavelength. The dye, namely fluorescein and indocyanine green (ICG) binds to plasma proteins within the blood vessels, resulting in a fluorescent image of the vascularization.

Last decade fluorescein dye has been replaced by ICG due to its superior side effect profile, shorter half-life, and being FDA approved. Information it can provide is dependent on the wavelength of the dye . ICG visualize vessels under the skin surface to approximately 10 mm deep.[24] FA has demonstrated useful in other specialties, and currently, numerous commercial near-infrared (NIR) light detection devices can be used.[24-32]

In breast reconstructive surgery, ICG angiography is most frequently used intraoperatively, but it is also used for flap monitoring.[33,34] Its main impact has been in the early identification of mastectomy skin flap necrosis to reduce postoperative complications.[33,35-38] Following isolation of the flap on its perforators, ICG angiography supports the clinical decision of which perforator(s) to base the flap on. This could be verified by placing and releasing sequentially vascular clamps on the perforators and scanning the perforasome.[39] Imaging following the completion of anastomosis can demonstrate good arterial and venous patency and support the clinical judgment about which part of the flap is poor perfused and should be discarded during flap trimming.[40-43]

A sparsity of studies investigating ICG angiography for perforator imaging. Azuma et al. performed a preoperative ICG angiography of the donor site and detected two to six subcutaneous perforator arteries in all 14 patients.[44] The location of the preoperatively marked perforators correlated well with the intraoperative findings; however, no specification has been given. They state ICG angiography to be more precise in the identification of perforator location than CTA, but do notify the drawback of only outlining the very superficial blood vessels. Visualization of perforators at greater depth is difficult to distinguish from deeper arteries and muscular branches and with that higher false-positive results. Pestana et al. compared in a prospective study of candidates for TRAM/DIEP flaps, the preoperative ICG-angiography perforator location, size, and blush intensity with CTA perforator location.[45] No correlation has been found. Reasonably, patients indicated for an abdominal-based breast reconstruction require a considerable amount of abdominal surplus. With a maximum penetration depth of infrared light at a maximum of 10 mm, ICG angiography can only provide information at the level of superficial tissue, and it is not sensitive or specific enough to detect perforators at the height of the fascia.

FA is a quick, non-invasive modality, imaging only the superficial vasculature and for that most suitable for tissue perfusion assessment. Little evidence has been found for FA in perforator mapping.

Dynamic Infrared Thermography

DIRT is an imaging technique based on skin temperature obtained via an infrared camera. After surface cooling, the temperature difference is analyzed during the rewarming phase. Different cooling methods are described; hemostatic clamps to block blood flow, applying cold water packs, blowing cooled air, extraction of heat by evaporation of alcohol from the skin.[46] Thiessen et al. standardized the measurement set-up and preferred 3 min cooling with 5 °C water in a sterile bag. This should obtain optimal cooling, preserve environment sterility and prevent tissue damage.[47]

Variables such as the rate of rewarming and the associated pattern reveal the so-called hotspots, indicating the locations of perforators that transport blood to the subdermal plexus. This technology is non-invasive and requires no contrast agents or radiation. DIRT has shown its use intraoperatively in multiple studies.[48,49] After perforator dissection but before pedicle ligation, thromboembolic events can be analyzed by the rate and pattern of rewarming.[50] Patency after microvascular anastomosis and flap perfusion can be visualized.[51,52]

There is limited evidence on the efficacy of DIRT for pre- and intraoperative perforator selection. De Weerd et al. reported on the value of the use of DIRT in the preoperative planning of the DIEP flap.[53] The rate of rewarming was critical to perforator selection, with the first appearing hotspots closely associated with the location of an arterial Doppler sound and intraoperatively with perforators passing through the tendinous intersection of the rectus. This was followed by another significant contribution from the Weerd et al. building on previous work, they systematically compared DIRT with CTA in 25 patients scheduled for a DIEP breast reconstruction.[54] Hundred and thirteen hotspots were registered using DIRT and 108 (95.6 %) corresponded to a perforator seen on CTA. In all cases, the selected perforator visualized with DIRT (the first appearing hotspot with the most progressive rewarming) was intraoperatively found to be the most suitable perforator. In a case report by Whitaker et al. in 2012, they compared DIRT with CTA and found matching results, but no accuracy has been given. They mentioned the possible advantage of DIRT in the context of remote ischemic preconditioning in the intraoperative setting.[55] Thiessen et al. compared 69 preoperatively marked hotspots with DIRT in 33 DIEP flaps with the intraoperative perforator location and found clinically matching results.[47,56] A total of 45 perforators were dissected. In case of multiple suitable perforators, the perforator with the best progressive rewarming was selected. They presented no accuracy about perforator location and subfascial course.

The latest maturation seen in DIRT is the smartphone-compatible miniature thermal imaging camera.[57,58] The resolution of the low-cost FLIR ONE© (FLIR Systems, Wilsonville, USA) is suboptimal compared to the more expensive thermal imaging cameras, but provides a quick screening tool that can be performed in the clinic with minimal training and can be carried in the pocket for ease of access.

DIRT could be valuable in selecting the most suitable perforators based on the rewarming pattern, defining perforasomes, and monitoring perfusion. This technology, although non-invasive and without the risk of intravenous contrast injection or exposure to ionizing radiation, needs an external device for tissue cooling and only provides a 2D map of the perforator vasculature. DIRT could be easily widely available and associated with lower costs, but there is limited evidence for its utility pre- and intraoperatively in perforator mapping.

Complementary techniques to perforating imaging modalities

Volumetric datasets (obtained by CTA or MRA) can be post-processed further to maintain all relevant information. Translating all this information in a more feasible way can help with the interpretation of radiologic findings. In the literature, various techniques have been described.

Image-guided stereotactic navigational systems

Image-guided stereotactic navigation systems give an accurate real-time correlation of anatomical locations to CTA or MRA imaging obtained preoperatively. Preoperative scans with fiducial markers placed on relatively fixed areas, such as bony landmark of the hip or scalp, are uploaded on a navigation system. Using the same fiducial markers, the navigation system can register the patient's anatomy and surgical instruments to the preoperative volumetric data, allowing real-time navigation through the image dataset. However, little published data exist regarding the use of these systems in plastic and reconstructive surgery.

Rozen et al. localized the DIEP perforators on the abdominal skin preoperatively with a navigation pointer connected to the navigation system.[59] Intraoperatively, the preoperative markings were seen within 5 mm of the perforator on the anterior rectus sheath. Results were compared to perforator localization transferred from conventional CTA images to the skin by an overlaid scaled 2D grid. In this small series, the use of image-guided stereotaxy was shown to be feasible and as accurate as CTA alone. Regarding the concerns of the suitability of fiducial marker fixation on non-bony landmarks, they have shown that this technology is feasible and accurate for other flaps such as the ALT flap.[60] Kocak et al. not only visualized where the surgical instruments were in relation to the preoperative CTA images, but were also able to visualize what was located 5, 10, and 15 mm ahead of the pointer.[61] This information results in more confidence and faster vascular dissection.

This technology is suitable for perforator imaging and navigation intraoperatively without reducing the accuracy compared to CTA, but the preparation of the system is time-consuming and the equipment itself, and its software are expensive and are thus only suitable for institutions with a large number of flaps in which the cost can be considered as a long-term investment.

Template

The most straightforward method to transfer CTA or MRA findings to the patient body is the use of a template. Scans are analyzed for perforator selection; the suitable perforators are marked onto a coronal-axis 2D grid at umbilical level at a subcutaneous plane just anterior to the rectus fascia. At the grid, holes are punched for marking the perforators. The grid with the representation of the abdominal wall is preoperatively centered on the umbilicus with the midline as reference points and perforators are marked.[62] Chae et al. compared the preoperative made grid with the intraoperative perforator location and found a statistically significant difference of 7 mm. Most discrepancies arose in the lateral row perforators.[63] In other studies, an error margin of less than 2.5 mm in distance between the umbilicus and the perforator has been reached.[64]

Later, Chae et al. did not only show the exit point of the perforators through the rectus fascia, but were also able to mark the DIEA pedicle and the intramuscular course of the perforators with a "DIEP template."[65] Moreover, they developed a "perforasome template" which could be placed on top of the "DIEP template" to mark the subcutaneous branches of each perforator.

These templates with an accuracy of a few millimeters are cheap, but mounting perforator locations on the grid and printing of the templates are time-consuming and do not give a 3D view.

3D printed anatomical model

The application of 3D printing is becoming increasingly popular in surgery to aid in the preoperative planning of complex procedures. In plastic surgery, Gillis and Morris introduced in 2014 the use of 3D printing for mapping perforator vessels.[66] Sotsuka et al. were the first to have it applied in breast reconstructive surgery.[67] They printed a 3D life-size model of the patient's perforator anatomy based on preoperative CTA data. The model was sterilized and used intraoperatively for a better understanding of the vascular anatomy. Mehta et al. and Jablonka et al. both printed an abdominal wall, with DIEP vessels and their course in relation to adjacent soft tissue and used it as a sophisticated educational tool.[68,69] Preoperatively, the model acts as a tool in surgical planning and intraoperatively as a point of reference to trace and follow the intramuscular course of the perforators. Ogunleye et al. drafted a comparable study with 58 patients. With their model, the surgeons deviate less often form their initial plan.[70] Moreover, during surgery fewer unnecessary maneuvers were made, which reduced flap harvest time with similar postoperative complications. At their institution, the added cost to print an abdominal 3D model is about $102. DeFazio et al. indicated with their preliminary results in 9 breast reconstruction patients, more accurate anatomy with regard to both deep inferior epigastric artery topography and perforator location when their 3D printed model was compared to CTA.[71]

Augmented reality

Plastic surgery is driven by visual data and is ideally suited to harness the features of AR in the clinical setting.[72] AR is the latest form of visualizing anatomy and has applications in a broad field, and it allows to render a prepared virtual model based on an imaging modality and displays it on top of the real world via means of electronic screens, projectors, or head-mounted devices

Projector-based augmented reality

Hummelink et al. developed a self-aligning hand-held projector, preoperatively displaying the location and intramuscular course of the artery perforators and subcutaneous branching on the patient's abdomen.[73] Using the three-dimensional reconstruction of the preoperative acquired CTA, the system shows the deep inferior epigastric artery, all significant perforators (diameter $>$ 1 mm), and highlights the perforators with the best location, shortest intramuscular course, and best subcutaneous branching. Additionally, flap volumes and lymph nodes can be displayed.[74,75] To transfer the virtual plan with automatic alignment to the patient's skin, the projector detects for global orientation four temporarily placed anatomic landmarks.

A randomized controlled trial with 60 patients was performed, and superior results were found compared to HHD.[76] The time preoperatively spent on obtaining a full perforator mapping took 20 and 2.3 min for measurements with bidirectional HHD device and the projection method, respectively. The number of perforators correctly identified intraoperatively was respectively 41.2% vs 61.7%, and flap harvest time could be reduced by 19 min. No difference in complication rate was seen.

Cifuentes et al. presented a projector-based method to display DIRT information on the patient, requiring manual alignment. Matching applied marker points and manual adjustment of the projector allowed for visualization of hotspots on the skin. This method provides less information compared to CTA, and accuracy was only correlated to Doppler.[77]

Wearable augmented reality

Pratt et al. utilized a wearable head system to overlay CTA images onto a patient extremity. They used the HoloLens (Microsoft, Redmond, WA, USA) to create a hologram by post-processing of preoperatively made CTA data and is able to visualize skin, bone, adipofacial tissue, muscle, and vascular models through the HoloLens. In six cases, the HoloLens was compared before and during the operation with Doppler without compromising environment sterility.[78] Superior results were found and considered as less time-consuming.

Wesselius et al. used the Microsoft HoloLens to visualize the epigastric arteries and their perforators in relation to the rectus abdominis muscle in preparation for a deep inferior epigastric perforator flap harvest.[79] A software application was developed to visualize the anatomy as a hologram and used abdominal nevi as natural landmarks. The three-dimensional holographic visualization provides an intuitive and strong perception of complex anatomy and can be used preoperatively to mark anatomic structures, such as vessels on the patients or intraoperatively to navigate. This workflow is of potential value to all kinds of flaps and to different surgical and medical specialties. Unfortunately, neither of them reported the accuracy of the hologram in breast surgery.

Discussion

Free flap autologous breast reconstruction has become a major part of the standard care in breast cancer. A presurgical vascular map assists in choosing the appropriate perforator. For years, Doppler, CTA, and MRA have been used intensively in perforator mapping. This study presents an up-to-date review on the spectrum of alternative perforator mapping modalities and the efficiency and utilization in the practice of free flap breast reconstructive surgery. The modalities were classified based on their concept of imaging as *volumetric perforator imaging, real-time perforator imaging*, and *complementary techniques*.

Volumetric perforator imaging (CTA, MRA) creates a bulk of data. Recently, artificial intelligence has been used for the automatic detection of dominant perforators seen on CTA and intends to simplify the work of health professionals and provide better outcomes.[80] However, volumetric datasets yield more data than just perforator locations and can be reconstructed into a highly detailed 3D vascular map. This bulk of information can be difficult to conceptualize and is in daily practice not used in its full potential. Complementary technologies aspire to make 3D data practical for direct vision pre- and intraoperative, resulting in a better understanding of the vascular anatomy during surgery. Utilizing information obtained with volumetric imaging techniques to full extend could result in more detailed reconstructions due to the increased knowledge of the surrounding tissue.

Many technologies are still in their infancy with only limited information available. Previously published reviews did not incorporate these novel techniques and sensitivity and specificity are often missing. To overcome this limitation, a large number of "MeSH" terms were used as part of the search strategy to ensure that all relevant studies were found and limiting the risk of selection bias. In this study, only articles concerning breast reconstructive surgery and perforator mapping were included. Technologies utilized in other fields of medicine may not have been identified.

Future research should be focused on obtaining more data regarding described novel imaging techniques and complementary technologies to volumetric imaging, ideally in terms of randomized controlled trials. AR is a promising and upcoming complementary technique to volumetric perforator imaging, steadily maturing and revealing its potential to the plastic surgical field, but further work to determine its accuracy and practicability is certainly warranted. It would be interesting to see how a combination of various imaging techniques complements each other in both perforator mapping and presentation to the clinician; e.g., AR featuring ICG imaging or dynamic infrared imaging. Furthermore, the resolution of volumetric imaging modalities has vastly improved over the years, and if this trend continues, structures such as nerves could be visualized, making innervated tissue harvest more convenient. Moreover, with 4D-CTA and 4D-MRA on the rise, this dynamic volumetric imaging may show insight into the perfusion of flaps prior to harvest, embedding technology even further into the field of plastic surgery.

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Conflict of interest/Competing interests

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Availability of data and material

The manuscript has not been submitted elsewhere. The references have been checked and are correct. For transparency and reproducibility, a full electronic search strategy for both databases has been added

Code availability

Not applicable

Authors' contributions

All the authors have been actively involved in the planning and enactment of the study and have also collaborated in the preparation of the paper.

S. Hummelink and D.J.O. Ulrich initiated the study, L.M. Steenbeek and K. Peperkamp performed the literature search, L.M Steenbeek performed data analysis and drafted the work, and S. Hummelink and D.J.O. Ulrich critically revised the work.

Ethics approval

Not required

Consent to participate

Not required

Consent for publication

The authors have read the "Guide for Authors" and the paper conforms to this guide in all respects. They have approved the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2022.06.100.

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