Intraoperative ultrasound guided breast surgery: paving the way for personalized surgery

Martin Espinosa-Bravo, Isabel T. Rubio

Breast Surgical Oncology, Breast Cancer Center, Hospital Universitario Vall d'Hebron, Barcelona, Spain Correspondence to: Isabel T. Rubio, MD, PhD. Breast Surgical Oncology, Breast Cancer Center, Hospital Universitario Vall d'Hebron, Paseo Vall d'Hebron 119, 08035 Barcelona, Spain. Email: irubio@vhio.net.

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Since the first publication in 1988 about intraoperative ultrasound (IOUS) guided surgery, where Schwartz and colleagues (1) found that ultrasound (US) was an accurate and effective tool for localizing breast masses visualized by US and thus facilitating the surgical excision, multiple manuscripts have reported the use of IOUS to guide BCS in non-palpable breast cancer (2-4).

The randomized trial study (5) comparing US guided lumpectomy of non-palpable breast cancer to needleguided resection (NL) showed that IOUS improved rates of margin positivity from 45% with NL alone to 11% with IOUS localization. But also the literature is replete with studies, largely retrospective, examining the advantages of IOUS that include increasing rates of negative margins, reducing the need for re-excision and decreasing patient's complications when compared to NL (2-7). Two metaanalysis have found similar results when examined rates of negative margins and need for re-excision that are improved with the use of IOUS (8,9), and yet, there continues to be debate regarding the advantages and the implementation of IOUS into the surgical management of breast cancer.

The use of IOUS has not only been reported to guide excision of non palpable breast cancer, (4) but also in UShematoma guided surgery (10), in patients with palpable tumors (3) and to guide BCS after neoadjuvant treatments (11). In all the scenarios, IOUS has obtained a good score.

The study by Haloua *et al.* (12) adds more information of the impact of IOUS guided surgery in the cosmetic outcomes and patient's satisfaction. The goal of breastconserving therapy is to excise the primary tumor with negative margins to minimize local recurrences and to preserve the shape and size of the breast for an optimal cosmetic outcome. There are several factors that determine the cosmetic outcome after BCS including the volume of resected breast tissue, radiotherapy dose, location of the tumor in the breast, type of incision, need of re-excision for margin control and postoperative complications such as wound infection (13,14).

In the randomized Cosmetic Outcome of the Breast After Lumpectomy Treatment (COBALT) trial (12) conducted in the Netherlands, the use of IOUS guided surgery is compared to palpation guided surgery in achieving better cosmetic results. They have shown that IOUS guided surgery significantly improves overall cosmetic outcomes and patient satisfaction at one year following surgery. Indeed, the cosmesis was better for the image-guided than for the palpation-guided surgery, as judged by a three-member panel blinded for the study arm, a computerized evaluation software (BCCT.core), and patient self-evaluation [odds ratio (OR) =0.55; P=0.067]. Overall, 'excellent' or 'good' cosmetic outcomes were reported for US-guided and palpable guided surgery in 72% and 65% of cases, respectively. Overall, a patient had a 45% reduced chance of a worse cosmetic outcome with US-guided compared with palpationguided surgery (OR =0.55; P=0.067); the odds of having a worse cosmetic outcome became significantly greater by 12 months (OR =2.57; P<0.001). This was primarily due to less volume of excision with US-guided BCS and less reexcision due to positive margins. The authors concluded that US-guided BCS for early-stage invasive breast cancer is superior to the standard palpation-guided surgery as it significantly lowers margin involvement rates, the need for additional therapy, and healthcare costs (although this datum is not presented in the report), improving overall cosmetic outcome and patient satisfaction. The importance of this study is the evidence that with this surgical approach there is also a positive patient's cosmetic results and experience.

Even though, it has been difficult to achieve a consensus on assessing cosmetic outcomes, to overcome this lacking, Haloua *et al.* (12) have included a range of objective and subjective evaluation methods to assess the appearance of the breasts. The analysis after 1 year maybe a good predictor although I encourage the authors to pursue long term follow up on cosmetic outcomes to confirm these optimal results. And as the authors report maintaining a favorable cosmetic outcomes, at the end favorably impact on the quality of life of patients.

Not to forget that, cosmetic result is one of the major determinants of psychological distress with large impact on body image, and studies have shown that women with poor cosmetic outcomes as determined by pronounced breast asymmetry and skin alterations are impaired in their selfesteem, feelings of sexuality and quality of life (13).

Another issue of concern has been rates of re-excision in BCS that can be as high as 40% (14). The ongoing mantra that extensive surgery or wider margins are correlated with better local control has come to an end with the publication of the consensus guidelines on margins by the Society of Surgical Oncology-American Society of Radiation Oncology (SSO-ASTRO) showing that there is no benefit for wider margins than "no ink on the tumor" in BCS (15). Therefore, there is no need to excise the tumor with a large volume of adjacent breast tissue, given that a large volume of resected breast tissue is the major determinant of a poor cosmetic outcome.

Accurate excision leads to a smaller and more precise volume of surrounding breast tissue removal without compromising the tumor-free margin. Traditionally in the clinical practice, the success of the removal of palpable breast cancer is based on pre-operative imaging techniques and the experience of the surgeon. Others advantages of the US-guided surgery in breast cancer is the ability to examine intraoperatively ex vivo the specimen and verify that the tumor has been excised. Using IOUS allows for a continuous visualization of the lesion during the entire surgical procedure. Ex vivo assess of margin status is also of great importance. Distance of the tumor to the margin can be US measured before sending the specimen for pathology. Re-excision of positive or very close margins by US intraoperatively has reduced the need for re-excision in a second surgical procedure.

It has also being shown that that during routine BCS,

an excessive volume of the breast tissue is excised in the majority of patients, and also in most cases presenting with a tumor-free margin, the tumor was located eccentrically in the excised volume, close to the nearest margin (16).

So accounting for these advantages, why is that IOUS has not been widely implemented yet? One should question if it is a matter of qualification. How do surgeons become qualified in intraoperative US-guided surgery? In the USA, the American Society of Breast Surgeons (ASBrS) offers breast ultrasonography certification to surgeons who meet the criteria in clinical experience, training, and quality assurance in this technique (17). Furthermore, the American College of Radiology (ACR) has now agreed to allow certification in breast ultrasonography by the ASBrS as one of the qualification options for physicians performing this technique in an ACR-accredited facility, confirming the importance and increased use of US-guided procedures performed by breast surgeons. In Europe, several courses on the use of IOUS are being held at different Institutions with expertise although still a certified qualification is not established. Breast surgeons have embraced new techniques that improve cosmetic results in breast cancer patients, as oncoplastic procedures, so certification in the use of IOUS should be also include in the armamentarium.

Evidence based medicine means using what works the best for the best value. Although there have not been many studies addressing costs of IOUs, the average cost of an IOUS was much less than NL (18). The cost differential between the procedures would favor IOUS as a means of localization. On the other hand, IOUS is performed by breast surgeons and thus avoiding the need for a separate invasive procedure. Surgeons should be encouraged to learn the skills needed to undertake intraoperative US-guided surgery. These skills will allow surgeons to achieve a higher surgical accuracy of breast-conserving surgery for breast cancer and improve cosmetic outcome and patient's quality of life. This and the next generation of breast surgeons will feel the way US is changing their surgical practice, and will aim to perform safer and more effective surgical procedures.

This editorial is not meant to suggest that other radioguided surgery may also be appropriate in guiding surgery. But available data support the greater advantages of IOUS guided surgery not only in improving surgical outcomes by achieving higher rates of negative margins, by reducing the need for re-excisions, but also showing better cosmetic results and patient's satisfaction, that all together conforms the success and place the IOUS guided surgery as the gold standard in guiding BCS in breast cancer. 368

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Footnote

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