EJGO European Journal of Gynaecological Oncology

Original Research

Magnetic seed localisation for non-palpable lesions in patients undergoing breast conservative surgery

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Summary

Purpose: Breast-conservative surgery is the standard procedure for breast cancer when tumour resection does not lead to significant cosmetic sequelae. The usual technique to locate non-palpable lesions is the wire-guided localization (WGL). However, the WGL may migrate and cause interference with the electro cautery. The placement of the WGL has to be performed on the day before or the day of the surgery, causing organizational problems. To optimize care pathway and increase ambulatory activity, the authors studied the feasibility and efficacy of a 5-mm iron seed MAGSEED. *Materials and Methods:* During four months, 20 seeds were placed in 19 patients undergoing a lumpectomy for non-palpable breast lesions. The evaluation questionnaire was filled by radiologists, surgeons, and patients. *Results:* All clips were detected. The radiological and surgical team found the MAGSEED simple and intuitive. Placement was done by ultrasound and stereotaxic guidance up to 15 days before surgery. Time of lumpectomy was reduced to an average of 11 minutes. Patients' pain level was low (2/10). *Conclusion:* The use of MAGSEED for the detection of non-palpable breast lesions is simple, safe, and feasible. A comparative randomized prospective study should be performed between MAGSEED and WGL to study the medico-economic outcomes and the surgical and radiological benefits of the magnetic seed.

Key words: Magnetic seed; Breast cancer; Localization; Wire; Lumpectomy.

Introduction

Breast-conservative surgery is the standard procedure for breast cancer when tumour resection does not lead to significant cosmetic sequelae. The usual technique to locate non-palpable lesions is the wire-guided localization (WGL) [1]. However, some difficulties may occur if the wire migrates before or during surgery, if the entry of the wire is at distance from the incision, or if the interference with the electrocautery causes thermal burn or even cuts the wire. The placement of the WGL has to be performed the day before or the day of the surgery, causing organizational problems for the patient and the medical team. Moreover, the patient may be intimidated by the metal wire protruding from the skin.

In order to reduce these difficulties, a radioactive seed localization (RSL) was developed for the first time in 2001, by Gray *et al.* [2]. The clip, a 4.5 by 0.8 mm titanium seed containing an I-125 dose of 0.050–0.300 mCi, could be placed up to 5-7 days before surgery and was localized during surgery by a gamma probe. The RSL offered many advantages for the hospital organization and in the operating theatre. As the seed could be placed few days before surgery and not necessarily the day or the day before surgery, the total hospital cost can be reduced by the possibility of ambulatory activity and reducing patient goings and comings. In the operating theatre, the surgeon was no longer constrained as with the wire. The seed allowed the surgeon the possibility to incise skin where he wanted without being bothered by the location or the wire protrusion; the seed localization also seemed more precise than the wire. Moreover, several studies have shown better cosmetic results, no significant difference for negative margin rates and schedule improvement compared to the WGL [3-6]. However the RSL is radioactive; therefore the manipulation of radioactive material requires a specialized structure and organization, from localization to excision, including transport, storage and elimination, increasing costs, and bringing constraints to diffusion of this technique [7-9].

In 2016, the FDA approved SAVI SCOUT radar localization system [8-10], a 12-mm non-radioactive seed detected by an infrared light probe. The device could be placed 30 days before surgery. However the SAVI SCOUT radar localization does not have the CE license and is relatively large compared to other clips (12 *vs.* 5 mm). Furthermore, the device contains nickel and should not be used if the patient is allergic. Also, detection can be difficult if the lesion is deeper than 6 cm or if there is a hematoma [10-11].

Recently, a non-radioactive device, MAGSEED, was

Published: 15 February 2020

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
XLI , n. 1, 2020
doi: 10.31083/j.ejgo.2020.01.4985

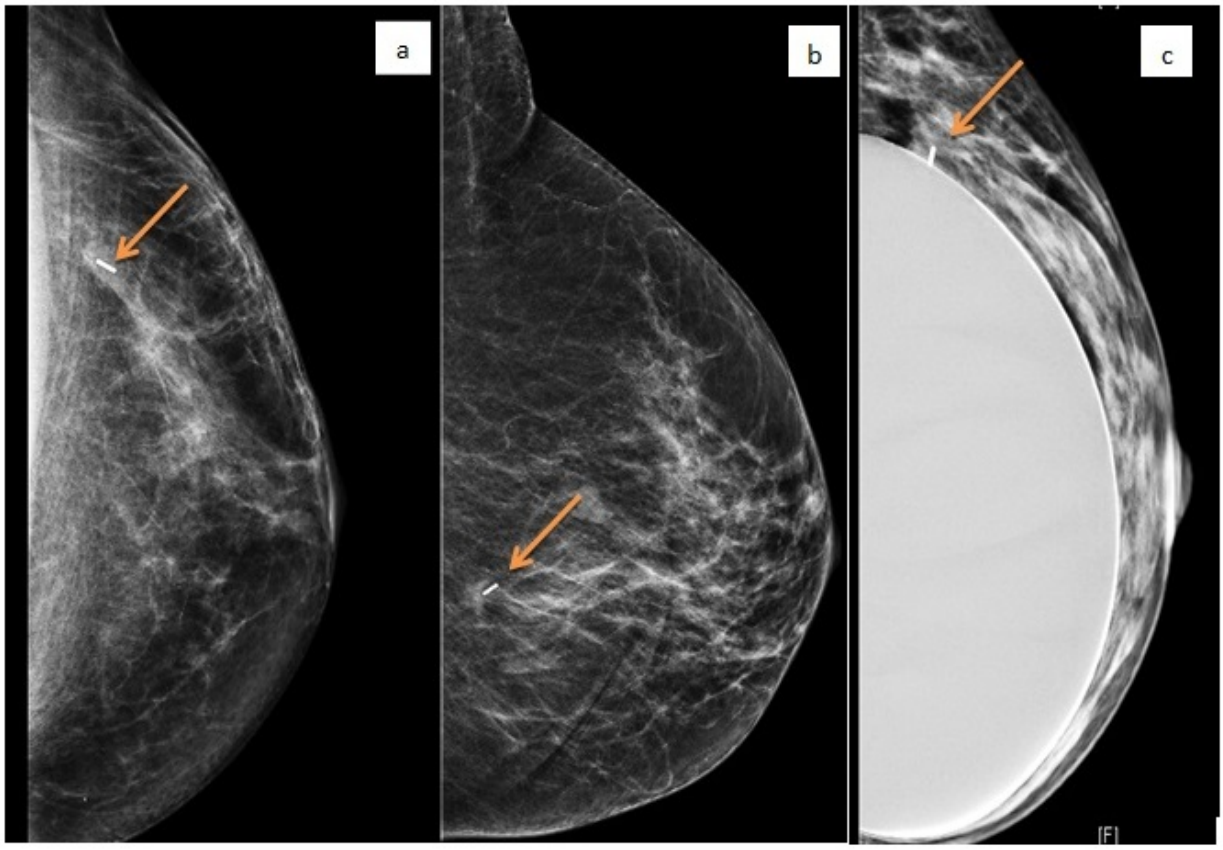

Figure 1. — Magseed localization performed under mammographic (a) or ultrasound (b-c) guidance, even in case of prosthetic implant (c).

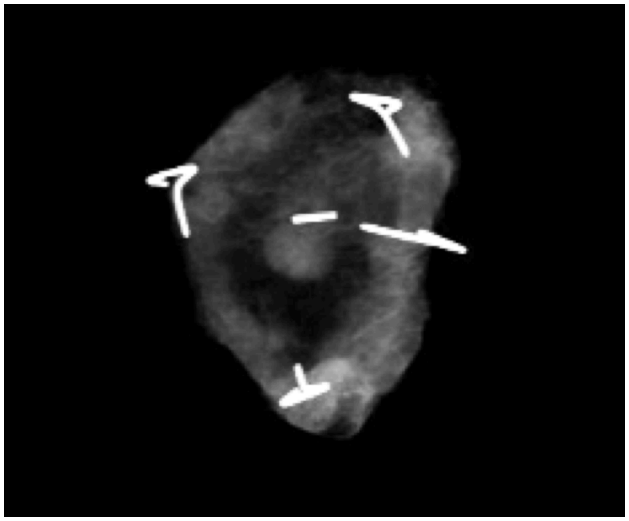

Figure 2. — Resected specimen radiogram.

developed and approved by both FDA and CE [9;12]. MAGSEED is a 5-mm iron seed placed by an 18-G needle introducer and detected at the operating theatre by a Sentimag magnetic probe. The only constraints are the need of non-ferromagnetic surgical retractors during surgery to avoid signal interference, and MRI artefacts.

The aim of this study was to assess the feasibility and precision of a non-radioactive ferromagnetic seed MAGSEED for non-palpable lesion localization in breast-conservative surgery in a small number of patients in France. The other criteria were the ease of use for the radiologist and surgeon, and the patient's pain during and after the localization procedure.

Materials and Methods

The study was authorized by the French Commission for Therapeutic Trials (Commission Scientifique des Essais Thérapeutiques, n. C.S.E.T.: 2018/2844). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

From March to June 2018, 19 patients with non-palpable breast lesions were included and 20 clips placed (one patient had two seeds placed for two different lesions). Patients with atypical lesions or T1-T2 non-palpable tumours with an indication of breast-conservative surgery were included during the preoperative consultation. Patients with T3-T4 tumours, pacemaker or other ferromagnetic device were excluded. Consent was not necessary because Magseed already had the CE marking.

The magnetic seed placement was performed on the day of the preoperative anaesthetic consultation to avoid multiple trips and

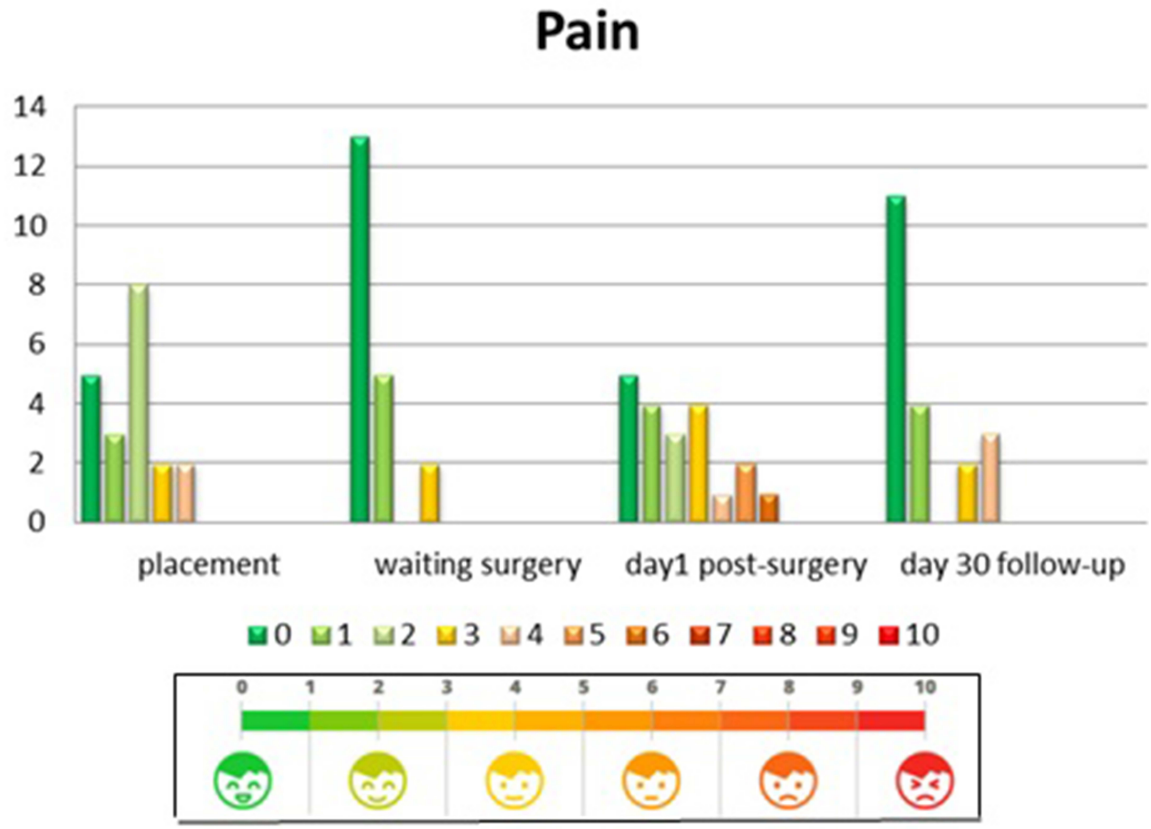

Figure 3. — Patient's pain scale. Pain's evaluation during different steps: seed placement, waiting time from surgery, first postoperative day, and follow-up.

additional costs. Figure 1 shows typical mammography after placement. Radiologists choose the point of entry regardless of surgeon incision. An evaluation questionnaire was filled by the radiologist for each procedure.

At the operating theatre before incision, the seed was detected with a dedicated Sentimag probe. During surgical excision, non-ferromagnetic retractors were used so as not to cause interference with the Magseed detection. Radiography of the specimen was performed during the surgical procedure to assess the location of the seed relative to the margins (Figure 2). An evaluation questionnaire was completed by the surgeon after each procedure.

Medical pain scale (0, absence of pain; to 10, maximum pain) (Figure 3) and a satisfaction questionnaire (Linkert scale: 1 not satisfied, 5 completely satisfied) was filled by the patient at each step: seed placement, waiting time for surgery, postoperative visit at day 30. Follow-up ended at day 30 (postoperative visit).

Results

Nineteen patients were included. Inclusion criteria were: age >18, lumpectomy for non-palpable lesions (tumor or atypical lesions), and absence of pacemaker or other ferromagnetic devices in patient's thoracic wall. The average patient age was 58 (range 36-77) years and the mean BMI was 25 (range 19-37).

Magseed was placed by ten different radiologists in a period of 0 to 15 days before surgery, with an average delay of three days. The average time of placement was eight (range: 2-20) minutes. The longest time was for a complex case of double stereotaxic identification in a fatty breast. The average depth (from the skin to the lesion) was 14 (range 5-35) mm.

Placement of the seed was performed by ultrasound guidance in 12 (60%) cases and by stereotaxic in eight (40%) cases. Radiologists considered the precision of clip location identical to the wire in 11 (55%) cases, better in 8 (40%), and less in only one (5%) case. The procedure seemed simpler than with the wire in 11 (55%) cases and identical in 9 (45%) cases; no radiologist evaluated the technique less than good.

Six surgeons from the Department of Breast Surgery at Gustave Roussy Institute operated the 19 patients. Intervention consisted in a lumpectomy and sentinel lymph node in 15 (75%) cases, simple lumpectomy in three (15%) cases, and lumpectomy with axillary lymph node dissection in the last two (10%) cases. In one case, two seeds were

Table 1. — *Study data.*

Age (years)	58 (range 36-77)
BMI (kg/m²)	25 (range 19-37)
Histology	
Ductal carcinoma	12 (60%)[1]
Lobular carcinoma	2 (10%)
DCIS	4 (20%)[2]
Fibroadenoma	1 (5%)
Atypical hyperplasia	1 (5%)
Margins	
Negative	18 (90%)
Positive	2 (10%)
Size	
Tumour (mm)	13 (range 0-32)
Lumpectomy (mm)	56 (range 30-90)
Participants	
Radiologists	10
Surgeons	6
Guidance modality	
Ultrasounds	13 (65%)
Mammography	7 (35%)
Surgery	
Oncoplastic incision	10 (50%)
Direct/periareolar incision	10 (50%)
Timing	
Placement (minutes)	8 (range 2-20)
Lumpectomy (minutes)	11 (range 7-16)

placed for two different lesions. Two procedures were performed after neoadjuvant chemotherapy by locating the biopsy clip by stereotaxic. All clips were detected without any problem. Half of the cases had a direct incision and the other half oncoplasty techniques (inverted T, round block, batwing).

The average lumpectomy surgery time (skin incision to tumour excision) was 11 (range: 7-16) minutes. The total length of surgery (from incision to closure) was 66 (range: 25-163) minutes. The shortest time of surgery was for a simple lumpectomy, whereas the longest time was for an oncoplasty technique with sentinel lymph node and contralateral symmetrisation. The surgical procedure was evaluated simpler by the surgeons compared to WGL in all cases.

The final histological results was infiltrating ductal carcinoma in 12 (60%) cases, invasive lobular carcinoma in two (10%) cases, ductal carcinoma in situ in four (20%) cases, atypical cylindrical metaplasia in one (5%) case, and fibroadenoma in one (5%) case. Two patients had neoadjuvant chemotherapy: in these two (10%) cases there was a complete response; therefore no cancerous cells were found. The target was then the titanium clip placed before chemotherapy. The average tumour size, understood as the longest dimension of the specimen, was 13 (range 0-32) mm for an average lumpectomy size of 56 (range 30-90) mm. Two patients had a complementary margin excision (10%) for an extensive ductal carcinoma in situ at the definitive analysis. An overview of all these data can be found in Table 1.

The patients filled a satisfaction and pain questionnaire. Concerning satisfaction, they showed a global acceptance of care, with a correct waiting time with an overall average rating of 4/5. During insertion of the MAGSEED, the pain score was less than 2/10 for 80% of the patients, the maximum score being 4/10 for two cases. During the waiting time, 13 patients (65%) had a score of 0/10; 5 (25%) had 1/10 and two cases 3/10 (Figure 3).

Finally a test was performed with a clip placed in a specimen to evaluate the risk of artefacts; if the seed is placed in patients undergoing MRI showing a 5-cm MRI artefact, spread could then interfere with lecture and diagnosis.

Discussion

Breast-conservative surgery is the standard procedure for the treatment of breast cancer when the tumour excision is relatively small compared to the breast volume, allowing good aesthetic results. The constant improvements in mammographic and other medical imaging techniques has made it possible to detect smaller lesions, resulting in the challenge to identify and remove these lesions while preserving a good aesthetic outcome.

At present, the most used technique to detect non-palpable breast cancer is the WGL [1]. However it has some disadvantages. For patients, the complications include pain, hematoma, syncope, pneumothorax, sight of a metallic wire protruding from the skin, risk of displacement if movement or pressure on the breast, discomfort due to a large bandage; for the radiologist, difficulty of placement, risk of migration; for the surgeon, necessity to undermine the skin to the entrance of the wire, influencing the type and location of incision, risk of displacement during oncoplasty and mammostat use, intraoperative wire transection, retention of a fragment, thermal injury caused by electrocautery contact; for the hospital organization, necessity to introduce the wire the same day or day before the surgery.

Thus, other techniques of localizations have been developed. Recently, a 5-mm ferromagnetic non-radioactive seed MAGSEED has been approved by the FDA and the CE. The procedure can be performed up until 30 days before surgery and according to previous studies it appears to be a precise, effective, simple, and intuitive technique for surgeons and radiologists.

The use of a magnetic seed was first described in 2017 by Schermers *et al.* of the Netherlands Cancer Institute [13]. In their experience, 15 non-palpable lesions were localized by both magnetic and radioactive seeds. The identification rate was 100 % and radiologists and surgeons found the magnetic seed intuitive, safe, and feasible. Price *et al.* [14] of University of California San Francisco published in February 2018 their early clinical experience of 73 magnetic seeds, with enthusiastic results concerning accuracy, efficacy and easiness.

Finally a clinical trial leaded by Harvey *et al.* [15] studied the risk of MAGSEED migration. Twenty-nine magnetic seeds were placed in 28 patients who underwent total mastectomy. The precision of the localization and the absence of device migration were confirmed by radiologists (by mammography), surgeons (by Sentimag probe during surgery) and pathologists (by specimen analysis).

To date, two clinical trials are on-going at MD Anderson Cancer Center: the first is a post-marketing study to provide prospective evidence that MAGSEED is effective for lesion localization and summarize measures of product safety and performance (NCT03020888); the second is a clinical study using MAGSEED to locate metastatic lymph nodes before their removal (NCT03038152) [16, 17]. Another trial is ongoing in the Netherland [18]. Thereby, if we consider the promising data of the first trials, the present authors wanted to study in the Gustave Roussy Cancer Institute the feasibility and efficacy of the MAGSEED technique through a pilot phase of 20 cases in which both radiologists and surgeons could get acquainted with the magnetic localization device.

Results of the present pilot phase were hopeful, with 100% magnetic clip detection. All surgical, radiological, and pathological team were satisfied with this technique. The radiologists found the MAGSEED simpler than the WGL in 55% and identical in 45%. The average seed insertion time was eight minutes and decreases to two minutes with US guidance.

The surgeons found this technique more practical, considering it simpler performing surgery and preoperative organization. At the operating room, after an initial learning curve phase, the average incision-to-tumour excision time was 11 minutes. The Duret's ridges' undermining was faster and simpler due to the absence of wire, and the type of incision or oncoplasty technique was not influenced by the location of the seed, which is in some cases compromised with the WGL, because sometime radiologists introduce the wire far from the lesion according to patient's position, especially in case of stereotaxic placement.

As MAGSEED is a non-radioactive device; there is no need of a nuclear department for regulation, placement and storage, facilitating greatly the acquisition, and use in hospitals without nuclear unit. Patients were also globally satisfied, and the pain level at device insertion and surgery waiting time was very acceptable. However, MAGSEED is an iron device, and in order to avoid signal interference with the Sentimag probe, non-ferromagnetic surgical retractors must be used, especially for small incisions. Thus, when oncoplasty incisions were used, the present authors did not require the retractors.

The magnetic clip does not migrate during MRI but causes artefacts into an area of 5 cm. Thus MRI should not be used for breast imaging but can be used to explore other body parts.

The total device cost including magnetic clip, installation system and non-ferromagnetic retractors, was about 350 Euro per patient, which is more expensive than the WGL estimated around 90 Euro. However, the MAGSEED allowed a better optimized organization, more ambulatory activity, no need of nuclear unit, a faster surgical intervention and less patient goings and comings, reducing the overall cost of the procedure in the economical evaluation schedule made by the economist of our institute. Nevertheless a comparative randomized prospective study should be conducted between MAGSEED and WGL to better study the medico-economic outcomes and the surgical and radiological benefits of the magnetic seed.

Conclusion

MAGSEED is a simple and feasible technique. In agreement with the data of the present authors' first preliminary phase, the MAGSEED technique consents short lumpectomy time and improves the care pathway and organization of both radiological and surgical team.

References

[1] Chan B.K., Wiseberg-Firtell J.A., Jois R.H., Jensen K., Audisio R.A.: "Localization techniques for guided surgical excision of non-palpable breast lesions". *Cochrane Database Syst. Rev.*, 2015, *12*, CD009206.

[2] Gray R.J., Salud C., Nguyen K., Dauway E., Friedland J., Berman C., *et al.*: "Randomized prospectie evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization". *Ann. Surg. Oncol.*, 2001, *8*, 711.

[3] Lovrics P.J., Goldsmith C.H., Hodgson N., McCready D., Gohla G., Boylan C., *et al.*: "A multicentered, randomized, controlled trial comparing radioguided seed localization to standard wire localization for nonpalpable, invasive and in situ breast carcinomas". *Ann. Surg. Oncol.*, 2011, *18*, 3407.

[4] Sharek D., Zuley M.L., Zhang J.Y., Soran A., Ahrendt G.M., Ganott M.A.: "Radioactive seed localization versus wire localization for lumpectomies: a comparison of outcomes". *AJR Am. J. Roentgenol.*, 2015, *204*, 872.

[5] McGhan L.J., McKeever S.C., Pockaj B.A., Wasif N., Giurescu M.E., Walton H.A., Gray R.J.: "Radioactive seed localization for nonpalpable breast lesions: review of 1,000 consecutive procedures at a single institution". *Ann. Surg. Oncol.*, 2011, *18*, 3096.

[6] Bloomquist E.V., Ajkay N., Patil S., Collett A.E., Frazier T.G., Barrio A.V.: "A Randomized Prospective Comparison of Patient-Assessed Satisfaction and Clinical Outcomes with Radioactive Seed Localization versus Wire Localization". *Breast J.*, 2016, *22*, 151.

[7] Jakub J., Gray R.: "Starting a Radioactive Seed Localization Program". *Ann. Surg. Oncol.*, 2015, *22*, 3197.

[8] Cheang E., Ha R., Thornton C.M., Mango V.L.: "Innovations in image guided preoperative breast lesion localization". *Br. J. Radiol.*, 2018, *91*, 20170740

[9] Jeffries D.O., Dossett L.A., Jorns J.M.: "Localization for Breast Surgery: The Next Generation". *Arch. Pathol. Lab. Med.*, 2017, *141*, 1324.

[10] Cox C.E., Garcia-Henriquez N., Glancy M.J., Whitworth P., Cox J.M., Themar-Geck M., *et al.*: "Pilot Study of a New Nonradioactive Surgical Guidance Technology for Locating Nonpalpable Breast Lesions". *Ann. Surg. Oncol.*, 2016, *23*, 1824.

[11] Mango V., Ha R., Gomberawalla A., Wynn R., Feldman S.: "Evalu-

ation of the SAVI SCOUT Surgical Guidance System for Localization and Excision of Nonpalpable Breast Lesions: A Feasibility Study". *AJR Am. J. Roentgenol.*, 2016, *15*, W1.

[12] Hayes M.K.: "Update on Preoperative Breast Localization". *Radiol. Clin. N. Am.*, 2017, *55*, 591.

[13] Schermers B., van der Hage J.A., Loo C.E., Vrancken Peeters M.T.F.D., Winter-Warnars H.A.O., van Duijnhoven F., *et al.*: "Feasibility of magnetic marker localisation for non-palpable breast cancer". *Breast*, 2017, *33*, 50.

[14] Price E.R., Khoury A.L., Esserman L.J., Joe B.N., Alvarado M.D.: "Initial Clinical Experience with an Inducible Magnetic Seed System for Preoperative Breast Lesion Localization". *AJR Am. J. Roentgenol.*, 2018, *210*, 913.

[15] Harvey J.R., Lim Y., Murphy J., Howe M., Morris J., Goyal A., Maxwell A.J.: "Safety and feasibility of breast lesion localization using magnetic seeds (Magseed): a multi-centre, open-label cohort study". *Breast Cancer Res. Treat.*, 2018, *169*, 531.

[16] Magseed Magnetic Marker Localization. ClinicalTrials.gov Identifier: NCT03020888. Available at: https://clinicaltrials.gov/ct2/show/NCT03020888

[17] Study the Use of Magseed and Sentimag to Localize Axillary Lymph Nodes. ClinicalTrials.gov Identifier: NCT03038152. Available at: https://clinicaltrials.gov/ct2/show/NCT03038152

[18] Magnetic Marker Localization for breast cancer surgery: An exploratory study. NTR NumberNTR6767. Available at: http://www.trialregister.nl/trialreg/ admin/rctview.asp?TC=6767

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