BJR
© 2018 The Authors. Published by the British Institute of Radiology
https://doi.org/10.1259/bjr.20170268

Received: 14 April 2017 | Revised: 19 October 2017 | Accepted: 23 October 2017

Cite this article as:
Milligan R, Pieri A, Critchley A, Peace R, Lennard T, O'Donoghue J.M, et al. Radioactive seed localization compared with wire-guided localization of non-palpable breast carcinoma in breast conservation surgery— the first experience in the United Kingdom. *Br J Radiol* 2018; **91**: 20170268.

FULL PAPER

Radioactive seed localization compared with wire-guided localization of non-palpable breast carcinoma in breast conservation surgery— the first experience in the United Kingdom

[1]ROBERT MILLIGAN, FRCS, [1]ANDREW PIERI, FRCS , [1]ADAM CRITCHLEY, FRCS, [2]RICHARD PEACE, PhD, [1]TOM LENNARD, FRCS, [1]J.M. O'DONOGHUE, FRCS, [3]RACHEL HOWITT, FRCPath, [1]STEWART NICHOLSON, FRCS, [1]HENRY CAIN, FRCS, [2]GEORGE PETRIDES, FRCR and [2]NIDHI SIBAL, FRCR

[1]Department of Cellular Pathology, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK
[2]Department of Breast Surgery, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK
[3]Directorate of Radiology, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK

Address correspondence to: Mr Robert Milligan
E-mail: *robmilligan@doctors.org.uk*

Objective: In the UK, guidewires have traditionally been used for localization of non-palpable breast lesions in patients undergoing breast conservation surgery (BCS). Radioactive seed localization (RSL) using Iodine-125 seeds is an alternative localization method and involves inserting a titanium capsule, containing radioactive Iodine-125, into the breast lesion. We aim to demonstrate feasibility of RSL compared with guidewire-localization (GWL) for BCS in the UK.

Methods: Data were collected on 100 patients with non-palpable unifocal invasive carcinoma of the breast undergoing GWL WLE prior to the introduction of RSL and the first 100 patients treated with RSL WLE. Statistical comparisons were made using X^2-squared analysis or unpaired two-sample t-test. Significance was determined to be at $p \leq 0.05$.

Results: Mean total tumour size was 19.44 mm (range: 5–55) in the GWL group and 18.61 mm (range: 3.8–59) in the RSL group ($p = 0.548$), while mean total specimen excision weight was significantly lower in the RSL group; 31.55 g (range: 4.5–112) *vs* 37.42 g (range: 7.8–157.1) ($p = 0.018$). Although 15 patients had inadequate surgical resection margins in the GWL group compared the 13 in the RSL group (15 *vs* 13%, respectively, $p = 0.684$), 10 of the patients in the GWL group had invasive carcinoma present resulting in at least one positive margin compared with only 3 patients in the RSL group (10 *vs* 3%, respectively, $p = 0.045$).

Conclusion: In this study, RSL is shown to be non-inferior to the use of GWL for non-palpable carcinoma in patients undergoing BCS and we suggest that it could be introduced successfully in other breast units.

Advances in knowledge: Here we have demonstrated the use of RSL localization results in significant lower weight resection specimens of breast carcinoma when compared with a matched group using GWL, without any significant differences in oncological outcome between the groups.

INTRODUCTION

In the UK 21,195 breast cancers were diagnosed within the National Health Service Breast Screening Programme in the year 2013–2014. Many screen-detected breast cancers are impalpable which require localization to aid complete surgical excision. Incomplete surgical excision, is a significant risk factor for local recurrence, which is associated with increased mortalilty.[1,2]

In the UK, guidewires have traditionally been the preferred method for localization of non-palpable breast lesions in patients undergoing breast conservation surgery (BCS). Guidewires are typically inserted on the day of surgery by breast radiology teams using stereotactic or ultrasonographic guidance. Guidewire-localized wide local excision (GWL WLE) has rates of incomplete tumour excision ranging from 12 to 37 percent.[3–5]

The use of guidewires for BCS is associated with a number of problems for both staff and patients alike. Unpredictable workloads for radiologists and technical difficulties for surgeons may lead to poorer outcomes, such as incomplete

excision of tumour or failed day case surgery because of delays to the start of lists. The optimal surgical incision can be compromised due to the orientation of guidewire placement.

Radioactive seed localization (RSL) using Iodine-125 seeds is an attractive alternative to both GWL and ROLL. This technique involves pre-operatively inserting a titanium capsule, containing radioactive Iodine-125 and an internal gold marker, into the breast lesion. Excision is guided by gamma probe detection. A significant advantage of RSL over ROLL is the greater flexibility of seed insertion times as a result of the significantly longer half-life of Iodine-125 compared with Technetium-99m (59.4 days *vs* 6 h, respectively).

It is for these reasons that our breast unit has introduced RSL using Iodine-125 seeds for malignant non-palpable breast lesions in patients undergoing BCS in our routine practice. The aim of this study was to evaluate and compare the use of RSL and GWL in our high volume breast screening unit to identify whether RSL WLE is a feasible alternative to GWL WLE in the UK.

METHODS AND MATERIALS

Ethical approval was gained through the local Introduction of New Procedures Committee and an application made through the Administration of Radioactive Substances Advisory Committee (ARSAC) prior to introducing RSL, as this technique had not previously been used in the UK. Data were collected on 200 consecutive patients with non-palpable breast carcinoma undergoing BCS with pre-operative radiological localization. The first 100 patients underwent GWL WLE prior to the introduction of RSL and formed a historical control group for comparison with the first 100 patients treated with RSL WLE. Only patients with clinically non-palpable and histologically proven invasive carcinoma of the breast were included. Exclusion criteria for both groups were identical, to avoid bias, and included: lesions requiring multiple guidewires or Iodine-125 seeds, those with pre-invasive carcinoma without an invasive component, those undergoing therapeutic mammoplasty or diagnostic excision biopsy, and cases where neoadjuvant chemotherapy had resulted in radiological complete response. The rationale for excluding cases requiring multiple Iodine-125 seeds was that the ARSAC certificate at the time of the study allowed for only a single Iodine-125 seeds to be inserted into any patient. To avoid bias, cases requiring multiple guidewires were also excluded. All lesions were localized with ultrasound guidance, stipulated in our ARSAC certificate for Iodine-125 seeds, using either a single guidewire or single Iodine-125 seed. The guidewires used for localization were either X-Reidy Breast Lesion Localisation Needle™ (Cook Medical Europe Ltd., Europe Shared Service Centre, O'Halloran Road, National Technology Park, Limerick, Ireland) or Homer Mammalok™ [Angiotach (PBN MEDICALS Denmark A/S) Knud Bro Alle 3, DK-3660 Stenlose, Denmark] as is standard practice in our unit. Bard Medical supplied all Iodine-125 seeds with a reference activity of 7.4 MBq. Each patient in the GWL group had the guidewire inserted on the day of surgery; each patient in the RSL group had the Iodine-125 seeds inserted between 7 and 14 days pre-operatively, as stipulated in our ARSAC certificate. The Iodine-125 seeds were inserted a minimum of 7 days pre-operatively to reduce the risk of seed migration during surgery and excised at no later than 14 days to minimize the radiation dose to the patient. All patients attended pre-assessment appointments and had surgery performed under general anaesthetic, the majority as day cases. The WLE procedure was performed prior to Sentinel Lymph Node Biopsy (SLNB) in all cases. For RSL WLE cases, the Europrobe 3.0™ (Gammadata Instrument AB, PO Box 2034, SE-750 02 Uppsala, Sweden) gamma probe was set to the Iodine-125 setting for the WLE and then switched to the Technetium-99m setting for SLNB. All surgeons performing WLE surgery were considered competent to do so; all surgeons were supervised performing their first five RSL cases prior to being deemed competent to practice independently. GWL WLE was performed under the care of six consultant surgeons, with five going on to perform RSL. The single consultant surgeon who did not perform RSL WLE is retired from operative surgery. Local risk assessments and protocols were developed in the RSL group according to UK radiation legislation to ensure that all radioactive Iodine-125 seeds were accounted for at all times prior to insertion and following excision from the patient. All specimens were orientated on a KliniTray™ (Kilinika Medical GmbH, Achtzehnmorgenweg 6, 61250 Usingen, Germany) and sent for intraoperative radiological assessment. A consultant radiologist confirmed to the operating surgeon that the lesion appeared to have been adequately excised or if further tissue needed to be taken. In cases where subsequent cavity shaves were performed, all further specimens were orientated. All specimens were sent fresh and weighed in the pathology laboratory prior to inking. The total specimen weight recorded included the main specimen excision in addition to any cavity shaves. Local guidelines at the time of the study considered a 1 mm radial resection margin satisfactory for invasive carcinoma and 2 mm radial margin for pre-invasive carcinoma; positive margins were considered anything less than 1 and 2 mm, respectively. All post-operative histology was discussed at a breast multidisciplinary team meeting. Further surgery either by margin re-excision or completion mastectomy was performed on any patient with inadequate radial excision margins. All Iodine-125 seeds were safely returned to the supplier for decay and disposal after usage. It should be noted that the study group of the 100 RSL cases commenced with the very first RSL case performed in the unit so includes the "learning curve" patients for all the radiologists and surgeons involved.

Data collected included: total tumour size, histological type and grade, receptor status, total specimen excision weight, whether cavity shaves were performed, completeness of tumour excision, any axillary procedure performed, any secondary surgical procedure performed and post-operative complication rates. Tumour size and specimen weight were all measured in the pathology laboratory. Mean specimen weight to tumour size ratio was calculated by taking the mean of all the individual specimen weight to tumour size ratios in the RSL and GWL WLE groups, respectively. Statistical comparisons of the WGL and RSL groups were made using X^2-squared analysis for nominal variables and unpaired two-sample *t*-test for continuous variables. Significance was determined to be at $p \leq 0.05$.

Table 1. Demonstrating comparisons between WGL WLE and RSL WLE data

		WG WLE (n = 100)	RSL WLE (n = 100)	p value
Tumour Grade	1	44	42	0.775
	2	40	44	0.567
	3	16	14	0.692
Tumour Type	Invasive ductal carcinoma	75	78	0.616
	Invasive lobular carcinoma	7	11	0.323
	Other invasive carcinoma	18	11	0.159
Invasive carcinoma with associated DCIS		79	74	0.404
Oestrogen receptor positivity (ER+)		93	95	0.552
Human epidermal growth factor receptor positivity (HER 2+)		9	9	1
Axillary procedure performed	Sentinel lymph node biopsy	95	92	0.389
	Axillary lymph node dissection	1	4	0.174
	No axillary procedure	3	3	1
	Axillary node sample	1	1	1
Specimen excision margins	At least one positive margin	15	13	0.684
	Invasive carcinoma at margin	10	3	0.045
	DCIS at margin	5	10	0.179
Cavity shave	Performed	51	55	0.571
	Prevented a second procedure	4	12	0.045
Mean total tumour size (mm)		19.44	18.61	0.548
Mean total specimen weight (g)		37.42	31.55	0.018
Mean total specimen weight to total tumour size ratio		2.24	2.16	0.024
Complications	Wound infection requiring antibiotics	2	1	0.561
	Haematoma (non-surgical management)	3	0	0.081
	Seroma requiring aspiration	2	3	0.651
	Deep vein thrombosis	0	1	0.316
Further surgery to breast	Margin re-excision	14	11	0.521
	Completion mastectomy	1	3	0.312

RESULTS

There were no instances of incorrect seed insertion, seed migration, radiation incidents or loss of seeds during this study. Patients were well matched for tumour grade and type, associated ductal carcinoma *in situ*, receptor status, and axillary procedure performed (Table 1). While mean total tumour size was similar between the two study groups, 19.44 mm (range: 5–55) in the GWL group and 18.61 mm (range: 3.8–59) in the RSL group (p = 0.548), the mean total specimen excision weight was significantly lower in the RSL group; 31.55g (Range: 4.5–112) *vs* 37.42g (range: 7.8–157.1) (p = 0.018). Mean total specimen weight to total tumour size ratio was also lower in the RSL group compared with GWL group (2.16 *vs* 2.24, p = 0.024). Although 15 patients had inadequate surgical resection margins in the GWL group compared the 13 in the RSL group (15 *vs* 13%, respectively, p = 0.684), 10 of the patients in the GWL group had invasive carcinoma present resulting in at least one positive margin compared with only 3 patients in the RSL group (10 *vs* 3%, respectively, p = 0.045). Intraoperative cavity shaves were performed in a similar number of cases for the GWL and RSL groups (51 and 55, respectively) but obviated the need for a second operation in more patients in the RSL group (4 *vs* 12, p = 0.045). One patient in the RSL WLE group required margin re-excision followed by completion mastectomy; all other patients requiring further surgery to the breast were treated with a single procedure. There were no differences in wound complication rates between the two groups.

DISCUSSION

Guidewire directed WLE has been the gold standard for the removal of impalpable breast lesions for many years but poses

technical and organizational difficulties for breast radiology and surgical teams, and is potentially stressful for the patients because of the need to have guidewire placement on the same day as surgery. The unpredictable workload of guidewire insertions can create significant time and staffing pressures for the radiology team and, for surgeons, difficulties with theatre list planning and delayed commencement of the operating list if cases requiring GWL are placed first on the list can reduce operating theatre efficiency. Alternatively, placing patients planned for GWL WLE later on the operating list may result in unplanned overnight stays in hospital. Other technical considerations for the operating surgeon include the possibility of guidewire dislocation and difficulty locating the tip of the wire, and hence the target lesion, within the breast. Reported cases of transected guidewires during surgery demonstrate the potential for fragments of wire to remain in the breast.[6–8] With a change in practice towards oncoplastic breast surgery in the UK, smaller resection volumes and cosmetically sensitive incisions are used where possible to improve cosmetic outcomes following WLE. In cases of GWL WLE, the optimal point at which the guidewire enters the skin for localization may be significantly distant from the optimal incision for BCS. This may result in larger resection volumes or higher rates of incomplete tumour excision.[9]

Several breast units in the UK have experience in using Radioactive Occult Lesion Localisation (ROLL) to try and obviate some of the problems associated with GWL WLE. ROLL involves an injection of Technetium-99m nanocolloid intra-tumourally and excision is guided by gamma probe detection. Although studies have shown ROLL to be comparable to GWL WLE in terms of complete tumour excision and re-excision rates, ROLL can lead to larger excision volumes.[10] In addition, because Technetium-99m has a short half-life, approximately 6 h, injections are usually performed on the morning of surgery or the evening before. As with guidewire insertion, this can also lead to an unpredictable workload for the radiology team. In addition, Technetium-99m is mammographically occult, rendering it difficult to accurately check the localization with mammography, as would be standard practice following guidewire insertion. If readily available, single-photon emission CT could be used to check for the localization of Technetium-99m within the breast.

In RSL, a titanium capsule (4.5 × 0.8 mm) containing radioactive Iodine-125 and an internal gold marker is inserted into the breast lesion; like ROLL, its excision is guided by gamma probe detection. This technique was first described by Gray et al in 2001.[11] RSL has the distinct advantage that as the Iodine-125 seeds are radio-opaque, post-insertion mammography may be used to ensure satisfactory localization has been achieved. The half-life of Iodine-125 is 59.4 days, allowing seeds to be inserted much further in advance of surgery than with localization for GWL or ROLL. RSL allows a far more focal localization within the breast compared with ROLL due to the lack of dispersion of Technetium-99 into the surrounding tissues. RSL is performed using standard localization techniques (ultrasound or stereotactic) as would be used for guidewire-localization (ultrasound only in the current study) and so can be implemented in any breast radiology unit with these facilities.[12,13]

RSL has been shown to be comparable to ROLL with regard to margin status and re-excision rates and has been shown to be equivalent or superior when compared with margin status and re-excision rates for GWL WLE.[14–16] A review of 100 consecutive procedures at a single institution by Meghan et al has shown RSL to be an effective safe procedure with just 3 seeds (0.3%) not being deployed correctly on first attempt.[17] RSL has also been shown to expose patients and staff to only minimal levels of radiation.[18] Seed migration appears negligible at 0.9 mm irrespective of time *in situ*, lesion type, type of surgery or radiological localization method.[19] Reduced operative time with RSL WLE over GWL WLE has also been demonstrated, which, although small, may have practical relevance in high volume units.[20]

Our results demonstrate statistically significant lower specimen resection weights with RSL in comparison to GWL WLE without compromising oncological safety. There is a trend towards lower margin positivity with RSL WLE compared with GWL WLE, although this was did not reach statistical significance in this study. Interestingly, patients undergoing RSL WLE were statistically less likely to have invasive carcinoma comprising a positive margin than patients who underwent GWL WLE; we hypothethize that this may represent the superiority of RSL to allow the operating surgeon to accurately localize the tumour intra-operatively in comparison with GWL.

The use of RSL with Iodine-125 seeds represents an important advancement in the surgical management of non-palpable breast disease in patients undergoing breast-conserving surgery. Since its introduction in our breast unit, the breast surgeons, radiologists and pathologists are in agreement that it is preferable and offers greater benefits than GWL for both patients and the breast unit. The operating surgeons have found that their operating lists are now less likely to be delayed due to tumour localization, allowing appropriate day-case procedures, such as RSL WLE, to be placed early on the list. An added benefit of RSL WLE is that the operating surgeon no longer has to factor in a guidewire when planning the breast incision; given oncoplastic breast techniques, this allows greater choice of cosmetically sensitive incision, such as peri-areolar, lateral perimeter or infra-mammary fold.

Pouw et al report the simultaneous use of Iodine 125 seeds and SLNB using Technetium-99m is possible under standardized conditions.[21] None of the surgeons reported any difficulties in locating the Iodine-125 seed in the breast due to the Compton effect, where scatter from Technetium-99m used in SLNB has the potential to interfere with signal detected by the gamma probe from the Iodine-125 seed. We concur with the findings of Loverics et al, which demonstrated that surgeons ranked RSL WLE as easier than GWL WLE (p = 0.008) while radiologists did not report a difference in difficulty (p = 0.398).[20] The radiologists in our unit have also found that the allocated times for pre-operative RSL have reduced their unpredictable peaks in their workload. The techniques of Iodine-125 seed insertion, surgical excision and pathological removal

of the seed are relatively simple and comparable to GWL techniques.

An unexpected incidental finding was that two patients who attended for Iodine-125 seed insertion were found to have a second ipsilateral breast carcinoma on ultrasound assessment, which was not identified on previous breast imaging. Given the 7 to 14 day period between RSL and surgery, this allowed enough time for biopsies to be taken and processed and final surgical management determined prior to the planned operation date with no subsequent delay in treatment; in both cases a supplementary guidewire was inserted into the second tumour on the morning of surgery and patients proceeded with BCS. Both patients were excluded from the study.

This study is limited by its inclusion criteria, which do not fully represent our practice of all BCS in our unit using localization. This is due to our adherence of the initial ARSAC certificate in relation to the use of RSL using Iodine-125 seeds, which stated that all RSL must be performed using ultrasonographic guidance, rather the stereotactic guidance. We have since extended our certificate to include stereotactic RSL and the use of up to four Iodine-125 seeds in any one patient. This will allow the RSL localization of patients who have tumours that are not visible on ultrasound and also to perform therapeutic mammoplasty of non-palpable tumours without bracketing guidewires. Further studies including cases with the extended ARSAC certificate criteria will reduce sampling biases. We would hope to further extend this certificate in the future to allow Iodine-125 seeds to be inserted for longer periods of time, which would allow patients to undergo neoadjuvant chemotherapy with a seed *in situ*, which would obviate the need for localization after treatment when it can be difficult to identify the core of the tumour. In addition, an extension to our certificate to allow RSL of a proven diseased axillary lymph node could offer similar benefits in the neoadjuvant settling as describe by Donker et al.[22]

The introduction of RSL in our unit has shown benefit to radiologists, patients, surgeons, and pathologists and we hope to further formally analyse this with a larger study in the future. In this study, RSL is shown to be non-inferior to the use of GWL for non-palpable carcinoma in patients undergoing BCS, and we suggest that it could be introduced successfully in other breast units.

REFERENCES

1. Harris JR, Botnick L, Bloomer WD, Chaffey JT, Hellman S. Primary radiation therapy for early breast cancer: the experience at The Joint Center for Radiation Therapy. *Int J Radiat Oncol Biol Phys* 1981; **7**: 1549–52. doi: https://doi.org/10.1016/0360-3016(81)90087-0
2. Bartelink H, Horiot JC, Poortmans P, Struikmans H, Van den Bogaert W, Barillot I, et al. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. *N Engl J Med* 2001; **345**: 1378–87. doi: https://doi.org/10.1056/NEJMoa010874
3. Tafra L, Fine R, Whitworth P, Berry M, Woods J, Ekbom G, et al. Prospective randomized study comparing cryo-assisted and needle-wire localization of ultrasound-visible breast tumors. *Am J Surg* 2006; **192**: 462–70. doi: https://doi.org/10.1016/j.amjsurg.2006.06.012
4. Mariscal Martínez A, Solà M, de Tudela AP, Julián JF, Fraile M, Vizcaya S, et al. Radioguided localization of nonpalpable breast cancer lesions: randomized comparison with wire localization in patients undergoing conservative surgery and sentinel node biopsy. *AJR Am J Roentgenol* 2009; **193**: 1001–9. doi: https://doi.org/10.2214/AJR.08.2005
5. Lovrics PJ, Cornacchi SD, Vora R, Goldsmith CH, Kahnamoui K. Systematic review of radioguided surgery for non-palpable breast cancer. *Eur J Surg Oncol* 2011; **37**: 388–97. doi: https://doi.org/10.1016/j.ejso.2011.01.018
6. Homer MJ. Transection of the localization hooked wire during breast biopsy. *AJR Am J Roentgenol* 1983; **141**: 929–30. doi: https://doi.org/10.2214/ajr.141.5.929
7. Montrey JS, Levy JA, Brenner RJ. Wire fragments after needle localization. *AJR Am J Roentgenol* 1996; **167**: 1267–9. doi: https://doi.org/10.2214/ajr.167.5.8911193
8. Bronstein AD, Kilcoyne RF, Moe RE. Complications of needle localization of foreign bodies and nonpalpable breast lesions. *Arch Surg* 1988; **123**: 775–9. doi: https://doi.org/10.1001/archsurg.1988.01400300121022
9. Fleming FJ, Hill AD, Mc Dermott EW, O'Doherty A, O'Higgins NJ, Quinn CM. Intraoperative margin assessment and re-excision rate in breast conserving surgery. *Eur J Surg Oncol* 2004; **30**: 233–7. doi: https://doi.org/10.1016/j.ejso.2003.11.008
10. Postma EL, Verkooijen HM, van Esser S, Hobbelink MG, van der Schelling GP, Koelemij R, et al. Efficacy of 'radioguided occult lesion localisation' (ROLL) versus 'wire-guided localisation' (WGL) in breast conserving surgery for non-palpable breast cancer: a randomised controlled multicentre trial. *Breast Cancer Res Treat* 2012; **136**: 469–78. doi: https://doi.org/10.1007/s10549-012-2225-z
11. Gray RJ, Salud C, Nguyen K, Dauway E, Friedland J, Berman C, et al. Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization. *Ann Surg Oncol* 2001; **8**: 711–5. doi: https://doi.org/10.1007/s10434-001-0711-3
12. Hughes JH, Mason MC, Gray RJ, McLaughlin SA, Degnim AC, Fulmer JT, Fulman JT, et al. A multi-site validation trial of radioactive seed localization as an alternative to wire localization. *Breast J* 2008; **14**: 153–7. doi: https://doi.org/10.1111/j.1524-4741.2007.00546.x
13. Rao R, Moldrem A, Sarode V, White J, Amen M, Rao M, et al. Experience with seed localization for nonpalpable breast lesions in a public health care system. *Ann Surg Oncol* 2010; **17**: 3241–6. doi: https://doi.org/10.1245/s10434-010-1139-4
14. van der Noordaa ME, Pengel KE, Groen E, van Werkhoven E, Rutgers EJ, Loo CE, et al. The use of radioactive iodine-125 seed localization in patients with non-palpable breast cancer: a comparison with the radioguided occult lesion localization with 99m technetium. *Eur J Surg*

Oncol 2015; **41**: 553–8. doi: https://doi.org/10.1016/j.ejso.2015.01.022

15. Sharek D, Zuley ML, Zhang JY, Soran A, Ahrendt GM, Ganott MA. Radioactive seed localization versus wire localization for lumpectomies: a comparison of outcomes. *AJR Am J Roentgenol* 2015; **204**: 872–7. doi: https://doi.org/10.2214/AJR.14.12743
16. Chiu JC, Ajmal S, Zhu X, Griffith E, Encarnacion T, Barr L. Radioactive seed localization of nonpalpable breast lesions in an academic comprehensive cancer program community hospital setting. *Am Surg* 2014; **80**: 675–9.
17. McGhan LJ, McKeever SC, Pockaj BA, Wasif N, Giurescu ME, Walton HA, et al. Radioactive seed localization for nonpalpable breast lesions: review of 1,000 consecutive procedures at a single institution. *Ann Surg Oncol* 2011; **18**: 3096–101. doi: https://doi.org/10.1245/s10434-011-1910-1
18. Pavlicek W, Walton HA, Karstaedt PJ, Gray RJ. Radiation safety with use of I-125 seeds for localization of nonpalpable breast lesions. *Acad Radiol* 2006; **13**: 909–15. doi: https://doi.org/10.1016/j.acra.2006.03.017
19. Alderliesten T, Loo CE, Pengel KE, Rutgers EJ, Gilhuijs KG, Vrancken Peeters MJ. Radioactive seed localization of breast lesions: an adequate localization method without seed migration. *Breast J* 2011; **17**: 594–601. doi: https://doi.org/10.1111/j.1524-4741.2011.01155.x
20. Lovrics PJ, Goldsmith CH, 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**: 3407–14. doi: https://doi.org/10.1245/s10434-011-1699-y
21. Pouw B, van der Ploeg IM, Muller SH, Valdés Olmos RA, Janssen-Pinkse LK, Oldenburg HS, et al. Simultaneous use of an (125)I-seed to guide tumour excision and (99m)Tc-nanocolloid for sentinel node biopsy in non-palpable breast-conserving surgery. *Eur J Surg Oncol* 2015; **41**: 71–8. doi: https://doi.org/10.1016/j.ejso.2014.10.046
22. Donker M, Straver ME, Wesseling J, Loo CE, Schot M, Drukker CA, et al. Marking Axillary Lymph Nodes With Radioactive Iodine Seeds for Axillary Staging After Neoadjuvant Systemic Treatment in Breast Cancer Patients. *Ann Surg* 2015; **261**: 378–82. doi: https://doi.org/10.1097/SLA.0000000000000558