Hong Kong J Radiol. 2024;27(3):e164-70. Published 10 September 2024 | https://doi.org/10.12809/hkjr2317719

ORIGINAL ARTICLE

Stereotactic-Guided Magnetic Seed Localisation Versus Radioguided Occult Lesion Localisation: A Comparison of Total Resection Volumes

RYS Mak[1], AHC Wong[1], CKM Mo[1], KH Chin[1], WWC Wong[1], PL Chau[2], YH Ling[2], LWY Ma[3], JSY Lee[3], JYW Chan[3], CY Choi[3], AYT Lai[1]

[1]*Department of Radiology, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China*
[2]*Department of Surgery, Ruttonjee Hospital, Hong Kong SAR, China*
[3]*Department of Surgery, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China*

ABSTRACT

Introduction: *Cosmetic outcome after breast conservation surgery has a major impact on patients' quality of life. Previous research demonstrated the use of non-radioactive magnetic markers (Magseed) to be safe and effective. There have been few studies comparing magnetic seeds and radioguided occult lesion localisation (ROLL). This study compares the total resection volume in lumpectomies of mammographically detected non-palpable lesions using magnetic seeds with the volume resulting from ROLL guidance.*

Methods: *This was a retrospective cohort study comparing lumpectomy cases guided by one or the other technique. Total resection volume was calculated based on pathology reports. Margin clearance and reoperation rates were analysed.*

Results: *Each cohort included 11 patients with similar baseline characteristics and comparable histopathology from the vacuum-assisted biopsy specimens. The technical success rates of magnetic seed deployment and ROLL injection were both 100%. The total resection volume in the magnetic seed cohort was significantly lower than that in the ROLL cohort. If the cases with involved or close margins were excluded from analysis of total resection volume, the magnetic seeds group still achieved a significantly lower total resection volume. No significant difference was found in the final histopathological diagnosis, margin clearance, or reoperation rates between the two groups.*

Conclusion: *Magnetic seed localisation is a safe and effective technique that can reduce total resection volume compared with ROLL, without compromising margin clearance and reoperation rates.*

Key Words: *Breast; Carcinoma; Psychosocial functioning*

Correspondence: *Dr RYS Mak, Department of Radiology, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China*
Email: mys877@ha.org.hk

Submitted: 4 April 2023; Accepted: 5 October 2023.

Contributors: RYSM and AYTL designed the study. RYSM, AHCW, CKMM, PLC, YHL, LWYM, JSYL, JYWC and AYTL acquired the data. RYSM, KHC, WWCW, YHL, LWYM and AYTL analysed the data. RYSM, AHCW and PLC drafted the manuscript. CKMM, KHC, WWCW, PLC, YHL, LWYM, JSYL, JYWC, CYC and AYTL critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of Interest: All authors have disclosed no conflicts of interest.

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability: All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics Approval: This research was approved by the Hong Kong East Cluster Research Ethics Committee of Hospital Authority, Hong Kong (Ref No.: HKECREC-2022-059). The requirement for patient consent was waived by the Committee due to the retrospective nature of the research.

Declaration: This paper was presented orally in the 30th Annual Scientific Meeting of Hong Kong College of Radiologists (12-13 November 2022; virtual meeting).

中文摘要

立體定位磁粒子定位與無線電導引隱匿性病灶定位：總切除體積的比較

麥恩善、黃可澄、巫冠文、錢凱、黃慧中、周珮鈴、凌若熙、馬慧欣、李雪盈、陳盈穎、蔡自怡、黎爾德

引言：乳房保留手術後的美容效果對患者的生活品質有重大影響。先前的研究證明使用非放射性磁性標記（Magseed）是安全有效的。比較磁性粒子和無線電引導隱匿性病灶定位（ROLL）的研究很少。本研究比較了使用磁粒子對乳房X光檢查檢測到的不可觸及病變進行腫塊切除術的總切除體積與ROLL引導結果的體積。

方法：這是一項回顧性隊列研究，比較由這兩種技術指導的腫瘤切除術病例。我們根據病理報告計算總切除體積，並分析切緣清除率和再手術率。

結果：每個隊列包括11名具有相似基線特徵和真空輔助活檢標本組織病理學相似的患者。磁粒子部署和ROLL注射的技術成功率均為100%。磁粒子組的總切除體積顯著低於ROLL組。如果將涉及或接近切緣的病例排除在總切除體積分析之外，磁粒子組的總切除體積仍顯著較低。兩組之間的最終組織病理學診斷、切緣清除或再手術率沒有顯著差異。

結論：磁粒子定位是一種安全有效的技術，與ROLL相比，可以減少總切除體積，且不影響切緣清除率和再手術率。

INTRODUCTION

The use of non-radioactive magnetic seed markers (Magseed; Endomagnetics, Cambridge, United Kingdom) is a relatively new technique for localisation of non-palpable breast lesions requiring surgical resection, including early breast cancers and high-risk lesions, which are being increasingly detected due to advancements in breast imaging techniques and more widespread breast cancer screening. Several studies have already demonstrated magnetic seeds to be a safe, effective method that is non-inferior to wire-guided localisation.[1-3] A recent retrospective cohort study showed that localisation with magnetic seeds resulted in reduced resection volumes without an increased margin positivity rate compared with wire-guided localisation. Minimising resection volumes is important for optimal cosmetic outcome.[4]

In contrast, there have been fewer studies comparing magnetic seeds and radioguided occult lesion localisation (ROLL). Initial experience in a regional hospital in Hong Kong showed comparable operation times, surgical specimen sizes, margin clearances and reoperation rates compared with ROLL, with magnetic seeds having the added advantage of being non-radioactive and allowing decoupling of radiological and surgical schedules.[5] Due to similar experience, magnetic seed localisation has become the preferred technique since its adoption in our unit.

It is known that the cosmetic outcome after breast conservation surgery (BCS) can affect the psychosocial functioning of patients.[6] Women with pronounced breast asymmetry are more likely to feel stigmatised, experience depressive symptoms, and have a worse quality of life.[6] The major determining factor for cosmetic outcome is resection volume.[7] Ideally, the resection volume should be as small as possible without jeopardising the margin status. This is in turn related to surgical accuracy that relies heavily on the localisation technique for non-palpable breast lesions.[7] We aim to compare the total resection volume along with other outcome measures, including margin status and reoperation rate, in lumpectomies of mammographically detected non-palpable lesions under magnetic seed and ROLL guidance performed in two regional hospitals in Hong Kong.

METHODS

This retrospective cohort study first identified all lumpectomy cases aiming at vacuum-assisted biopsy (VAB) markers guided by stereotactic-guided magnetic seed localisation. To control for the targeted amount of tissue to be excised, only the lumpectomy cases aiming at radiopaque VAB markers that were placed after VAB were included. These were malignant or high-risk lesions identified from the VAB specimens, which required further surgical excision. These excisions were guided by magnetic seed placement. The cases were then matched with a control group of older consecutive lumpectomy cases aiming at VAB markers stereotactically guided by ROLL, beginning immediately before the adoption of magnetic seeds for such cases, until the same number was reached. Theoretically, as the lesions were non-palpable and sonographically occult, and the VAB markers were the common mammographically localised targets, the expected total resection volume would be comparable between the two cohorts. It was not feasible to draw both cohorts from the same time period as ROLL was rarely utilised after the introduction of magnetic seeds.

Electronic medical records were reviewed. Baseline characteristics including age, laterality of lesion, initial mammographic abnormality, pathology of the VAB specimen, and the time interval between localisation and operation were recorded. The preoperative mammographically detected post-VAB residual lesion sizes including the VAB marker (3 mm) were measured. The total span of the preoperative mammographically detected post-VAB residual lesion (with inclusion of the VAB marker) and the localisation agent (magnetic seed or iodinated contrast injected during ROLL) was likewise measured.

Surgical specimen volume was calculated using the ellipse volume formula Volume = $4/3 \times \pi \times A \times B \times C$, where A, B, and C are the lengths of all three semi-axes as documented in the pathology reports. If additional margins were excised intraoperatively, their volumes were likewise calculated. In cases where intraoperative additional margins measurements were not fully documented, they were assumed to be of negligible volume. Specimens of other breast lesions, contralateral breast surgery, and sentinel lymph node biopsy were considered irrelevant in the calculation of specimen volume in this study. The total resection volume was yielded by the sum of all relevant specimens.

The technical success rate of localisation for magnetic seeds and ROLL were recorded. The technical success of magnetic seed localisation was defined as deployment of the seeds without significant migration (>1 cm), and subsequent excision of the seeds and the VAB marker. In the ROLL cohort, additional iodinated contrast (0.1-0.25 mL) was injected at the original site of isotope injection, followed by post-procedural mammographic spot images and planar scintigraphy to ensure accurate localisation and absence of ductograms. Technically successful ROLL was defined as iodinated contrast seen at the site of the VAB marker and its subsequent complete excision of the VAB marker.

Other relevant outcome measures, including operation duration, pathology of the lumpectomy specimen, margin status, successful surgical removal of all VAB markers and magnetic seeds, and reoperation within 6 months, were also analysed.

Statistical Analysis

Statistical analysis was performed using SPSS (Windows version 28.0; IBM Corp, Armonk [NY], United States). Graphical representations were made using commercial software GraphPad Prism (Windows version 9.3.1; GraphPad Software Inc, San Diego [CA], United States).

Frequencies and percentages were calculated for categorical data and compared using Fischer's exact test. Continuous data were reported as medians with interquartile range and compared using the Mann-Whitney *U* test.

RESULTS

A total of 11 consecutive lumpectomy cases with stereotactic guidance targeting VAB markers and localised with magnetic seeds were identified between 1 April 2021 and 28 February 2022, after excluding a case in which multiple lesions localised with magnetic seeds were excised in one specimen. A control group of 11 consecutive lumpectomy cases with stereotactic guidance targeting VAB markers managed with ROLL between 2 May 2019 and 31 March 2021 was identified. All lumpectomies were performed by at least one specialist surgeon. There were seven specialist surgeons in the magnetic seed cohort, two of whom performed the lumpectomies in the ROLL cohort.

Baseline characteristics of the patients and lesions in both groups are shown in Table 1. Both groups of patients had similar age ranges. All the lesions initially manifested as microcalcifications, with or without architectural distortion. The histopathology from the VAB specimens in both cohorts were comparable, with most lesions being either atypical ductal hyperplasia (ADH) or ductal carcinoma in situ (DCIS), and a minority of lobular carcinoma in situ or invasive ductal carcinoma. None of

Table 1. Baseline characteristics of patients and lesions localised with magnetic seeds or radioguided occult lesion localisation.*

	Magnetic seeds (n = 11)	ROLL (n = 11)	p Value
Age, y	59 (57-69)	62 (48-66)	0.847
Laterality			
Right	8 (72.7%)	6 (54.5%)	0.659
Left	3 (27.3%)	5 (45.5%)	
Initial mammographic abnormality			
Microcalcifications only	9 (81.8%)	11 (100%)	0.476
Microcalcifications with architectural distortion	2 (18.2%)	0	
Preoperative histopathological diagnosis from VAB			
LCIS	0	1 (9.1%)	0.473
ADH	6 (54.5%)	5 (45.5%)	
DCIS	3 (27.3%)	5 (45.5%)	
IDC	2 (18.2%)	0	
Time from localisation to operation, d	9 (4-10)	0 (0-0)	0.000

Abbreviations: ADH = atypical ductal hyperplasia; DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma; LCIS = lobular carcinoma in situ; ROLL = radioguided occult lesion localisation; VAB = vacuum-assisted biopsy.
* Data are shown as No. (%) or median (interquartile range), unless otherwise specified.

the patients included in the study received neoadjuvant treatment prior to lumpectomy.

The cases localised by magnetic seeds underwent lumpectomy with or without sentinel lymph node biopsy, with the magnetic seeds placed at a median of 9 days (interquartile range, 4-10) before surgery. All cases guided by ROLL underwent lumpectomy within the same day (Table 1).

The outcomes of the lumpectomy cases localised with magnetic seeds and ROLL are shown in Table 2. The technical success rates of marker deployment and ROLL injection were 100%. The preoperative mammographically detected post-VAB residual lesion size with inclusion of the VAB marker in both groups did not differ significantly (3 mm vs. 3 mm; $p = 0.652$). After localisation, the total span of the preoperative mammographically detected post-VAB residual lesion (with inclusion of the VAB marker) and the localisation agent (magnetic seed or iodinated contrast injected during ROLL) was significantly lower in the magnetic seed cohort compared with the ROLL cohort (6.5 mm vs. 15 mm; $p < 0.001$) [Table 2].

The median operative time was lower in the magnetic seed cohort compared with the ROLL cohort (32 min vs. 52 min; $p = 0.028$), after exclusion of the cases that also underwent sentinel lymph node biopsy, excision of additional breast lesion(s) or contralateral breast surgery in the same setting. However, there were six such excluded cases in the magnetic seed cohort and one in the ROLL cohort, rendering the sample size small (Table 2).

The total resection volume of the relevant specimens in the cases localised by magnetic seeds was significantly lower than in the group using ROLL (11.5 cm^3 vs. 21.2 cm^3; $p = 0.028$) [Table 2 and Figure]. If the cases with involved or close margins (three in the magnetic seed cohort and two in the ROLL cohort) were excluded from analysis, the magnetic seeds group still achieved a lower total resection volume (11.3 cm^3 vs. 25.2 cm^3; $p = 0.015$). There was a higher proportion of cases with additional margins resected intraoperatively in the magnetic seeds group (54.5% vs. 36.4%), but it did not reach statistical significance ($p = 0.670$) [Table 2]. In two cases of the ROLL cohort and one case in the magnetic seed cohort, the measurements of the additional margins taken were not fully documented and they were assumed to be of negligible volume.

There was no incidence of magnetic seed migration in the entire cohort. All magnetic seeds and VAB markers were successfully removed from all patients (Table 2).

The final histopathological diagnoses of the lesions, which were taken as the higher of the grades between the VAB and lumpectomy specimens, were comparable in both groups with no significant difference ($p = 0.565$) [Table 2]. Two cases in the magnetic seed group and one in the ROLL group were upgraded from ADH to DCIS after surgical excision.

The margin clearance rates (72.7% vs. 81.8%) and reoperation rates (18.2% vs. 18.2%) were similar in both groups with no statistically significant difference (both $p = 1.000$) [Table 2]. In all cases localised by magnetic

Table 2. Comparison between outcome measures of lumpectomy cases localised by magnetic seeds and radioguided occult lesion localisation.*

	Magnetic seeds (n = 11)	ROLL (n = 11)	p Value
Technically successful marker deployment or ROLL injection			
Yes	11 (100%)	11 (100%)	1.000
No	0	0	
Preoperative mammographically detected residual lesion size,† mm (IQR)	3 (3-5)	3 (3-14)	0.652
Total span of preoperative mammographically detected residual lesions† and localisation agent, mm (IQR)	6.5 (6-8)	15 (14-18)	< 0.001
Median duration of operation, min‡ (IQR)	32 (28.5-44)	52 (35-67.5)	0.028
Median total resection volume, cm^3 (IQR)	11.5 (8.2-15.8)	21.2 (12.8-46.2)	0.028
Median total resection volume after excluding involved/close margin cases, cm^3 (IQR)	11.3 (8.6-12.9)	25.2 (12.7-58.8)	0.015
Additional margin excised intraoperatively			
Yes	6 (54.5%)	4 (36.4%)	0.670
No	5 (45.5%)	7 (63.6%)	
All magnetic seeds and VAB markers removed			
Yes	11 (100%)	11 (100%)	1.000
No	0	0	
Final histopathological diagnosis			
LCIS	0	1 (9.1%)	0.565
ADH	4 (36.4%)	4 (36.4%)	
DCIS	5 (45.5%)	6 (54.5%)	
IDC	2 (18.2%)	0	
Involved or close margin§			
Yes	3 (27.3%)	2 (18.2%)	1.000
No	8 (72.7%)	9 (81.8%)	
Reoperation within 6 months (or up to the time of writing)			
Yes	2 (18.2%)	2 (18.2%)	1.000
No	9 (81.8%)	9 (81.8%)	

Abbreviations: ADH = atypical ductal hyperplasia; DCIS = ductal carcinoma in situ; IDC = invasive ductal carcinoma; IQR = interquartile range; LCIS = lobular carcinoma in situ; ROLL = radioguided occult lesion localisation; VAB = vacuum-assisted biopsy.

* Data are shown as No. (%), unless otherwise specified.

† With inclusion of VAB marker.

‡ Excluded six cases in the magnetic seed cohort and one case in the ROLL cohort that also underwent sentinel lymph node biopsy, excision of additional breast lesion(s) or contralateral breast surgery in the same setting.

§ 'Close margin' is defined as <2 mm for DCIS. For IDC, a clear ink margin is considered adequate.

seeds, there was no margin involvement. Two cases with DCIS did have close margins (<1 mm and 0.5 mm) and underwent re-excision of margin and mastectomy, respectively. No evidence of malignancy was detected in the subsequent specimens obtained in either case, except a small focus of ADH found in the patient who had mastectomy. One patient who had DCIS with a close margin (1.8 mm) opted against reoperation, proceeded to adjuvant radiotherapy and has remained in remission up to the time of this writing (9 months after her operation). No significant postoperative complications were recorded in the magnetic seed cohort. In the group localised with ROLL, one case of DCIS had focally involved margins and underwent re-excision. Residual DCIS was found in the re-excision specimen. There was one case of DCIS with a close margin (<1 mm) upon which a radiotherapy boost instead of re-excision was decided after multidisciplinary team discussion. One patient underwent wound exploration and clot evacuation due to postoperative hematoma.

DISCUSSION

This study showed that a statistically significant smaller total resection volume could be achieved with magnetic seed localisation compared with ROLL, while maintaining a similar margin clearance and reoperation rate (Table 2). Although additional margins were excised intraoperatively in a non-significantly higher proportion of cases in the magnetic seed group, it did not lead to an overall increased total resection volume, which is the main determinant for cosmetic outcome.[7] Previous studies on cosmetic outcomes after BCS found that exceeding a resection volume of 50 to 85 cm^3 was associated with a higher rate of cosmetic failure.[7-11] In our study, there was only one case in the magnetic seed cohort in which the total resection volume reached this

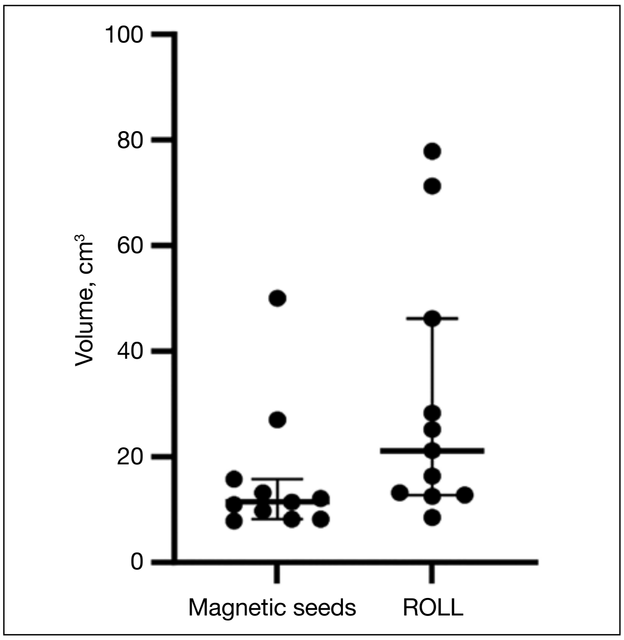

Figure. Column scatter graph of the total resection volume in the lumpectomy cases guided by magnetic seeds and radioguided occult lesion localisation. The median is represented with the interquartile range (horizontal lines). The difference between the two groups was significant (p = 0.028).
Abbreviation: ROLL = radioguided occult lesion localisation.

range (50.1 cm^3). Two cases from the ROLL cohort (77.8 cm^3 and 71.3 cm^3) fell within this range. None in the entire cohort exceeded 85 cm^3.

The magnetic seeds were placed at a median of 9 days before surgery. In contrast, all cases guided by ROLL underwent same-day operation due to the constraint of the nature of radioisotopes. Successful removal of the magnetic seeds from the patient was achieved in all cases (Table 1). The median operative time was lower in the magnetic seed cohort (Table 2). No complications were observed in the group localised with magnetic seeds, while there was one case of postoperative hematoma requiring surgical wound exploration in the group guided by ROLL.

A possible reason for the improvement in resection volume using magnetic seeds could be its ability to more precisely localise lesions, thus enhancing surgical accuracy. With ROLL, the radioisotope, and hence the area with highest radioactivity detected by the gamma probe, infiltrates and disperses to adjacent tissues upon injection, as supported by our data, resulting in the surgeons resecting additional margins if residual activity is detected in the surgical bed.[12] Intraductal injections can also occur in ROLL, causing the radioisotopes to be even more widely dispersed, in which case a salvage localisation procedure would be necessary.[7,13,14] Moreover, in the post-excision specimen radiograph, it is easier to visualise the centre of the target if it is guided by magnetic seeds than by ROLL.[15] One case from the ROLL cohort in the study took up to four specimen excisions before the VAB marker was seen included within one of the specimens. It is possible that the diffuse distribution of the radioisotopes could have contributed to the need for repeated excisions in this case. In comparison, a magnetic seed can pinpoint the exact location of a lesion. The main factor that could undermine its accuracy would be migration. Previous studies showed that magnetic seed migration appears to occur more frequently when performed under stereotactic guidance owing to the 'accordion' effect, which the release of breast compression causes the magnetic seed to migrate along the direction of compression.[16,17] This effect could be mitigated by using less compression before deploying the marker and by slowly releasing the breast from compression after placement.[17] The reported migration rates of magnetic seeds in previous studies were low[17-19]; none of the magnetic seeds migrated in this study.

Overall, the observations in this study echo those of previous works.[1-3,5] It shows that magnetic seeds are a safe and effective localisation technique, and further suggests that they can reduce total resection volume compared with ROLL, without negatively impacting the margin clearance and reoperation rates. They could potentially benefit patients with early-stage breast cancer, for which BCS with adjuvant radiotherapy is the standard treatment. This is a large group of patients with good survival rates, who face substantial psychological stress.[6,20] Although BCS preserves the breast, it results in different degrees of breast asymmetry, which runs the risk of affecting the psychosocial functioning of these surviving cancer patients.[6] Improving the cosmetic outcome without compromising the oncological margin status may contribute to their psychosocial well-being and quality of life.[7]

One major drawback of magnetic seeds is their high cost in comparison with ROLL and other localisation techniques, which may be a barrier to its adoption in some centres. The logistical advantage of magnetic seeds due to the decoupling of localisation and surgery may be able to reduce delays in surgery and increase overall efficiency.[7] Future cost-effectiveness analysis is required and should take into consideration the overall efficiency, which include surgical outcomes including cosmetic results and patient satisfaction.

Limitations

This study has several limitations. First, the sample size was small, including patients only from two regional hospitals, during the initial stage of magnetic seed adoption. Second, surgeons might have resected a larger amount of tissue in selected cases to ensure a clear margin, particularly if previous VAB pathology results already confirmed malignancy. This was assumed to be balanced out by the relatively comparable distribution of high risk versus malignant pathology of the VAB specimens in both cohorts. Contrary to the concern for selection bias, in the magnetic seed cohort of the current study, there were two more invasive cancer cases than in the ROLL cohort, which would presumably require a wider margin. Third, the specimen weights were not available in some cases, thus specimen volumes were retrospectively calculated using the ellipse volume formula, assuming that the surgical specimens were ellipsoids. In practice, however, they are often irregularly shaped. In a few cases, the measurements of some of the additional margins excised were not fully documented, which may affect the accuracy of the results.

CONCLUSION

This study demonstrated that localisation of non-palpable breast lesions with magnetic seeds can achieve a smaller total resection volume compared with ROLL, without affecting the margin clearance or reoperation rate. Multicentre studies with larger sample size are required to substantiate this finding and compare other surgical outcomes of magnetic seeds and ROLL.

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