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Original article

The introduction of radioactive seed localisation improves the oncological outcome of image guided breast conservation surgery

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ABSTRACT

Introduction: Radioactive seed localisation (RSL) has become increasingly popular for localisation of non-palpable breast tumours. This is largely due to advantages it offers in terms of practicality and convenience when compared to guide wire localisation (WL). This institute switched from using WL to RSL in September 2014. The primary aim was to assess whether this change improved the accuracy of excision with regards to inadequate margin rates and weight of excision specimens. The secondary aim was to establish whether there is a "learning curve" associated with RSL technique.

Methods: Retrospective data collection was performed for 333 consecutive cases of unifocal non-palpable invasive breast cancers undergoing excision with WL or RSL. An inadequate margin was defined as tumour <1 mm from an inked radial margin. Patient demographics, tumour characteristics and clinical outcomes were compared between WL and RSL cases.

Results: 100 WL and 233 RSL cases were included. Patient demographics and tumour characteristics were similar for both groups. Inadequate margin rates were 18% with WL and 8.6% with RSL ($p = 0.013$). Median specimen weights were 33.3 g with WL and 28.7 g with RSL ($p = 0.014$). Subdividing the RSL group into the first 100 cases performed (RSL1) and the subsequent 133 cases (RSL2), inadequate margin rates were 13.0% and 5.3% respectively ($p = 0.037$). Mean specimen weights were similar.

Conclusion: Switching from WL to RSL results in a significant reduction in both inadequate margin rates and specimen weights. A procedure-specific learning curve is present on first implementation of RSL and following this, inadequate margin rates are further reduced.

1. Introduction

In the UK, almost a third of breast cancers are diagnosed by the National Health Service Breast Screening Programme (NHSBSP) [1]. The majority of these tumours are non-palpable therefore requiring localisation to guide intra-operative tissue excision. In 1965, Dodd et al. first described a guide wire method of localisation which, by the late 1970s, had become widely established [2,3]. Almost forty years later, wire localisation (WL) still remains standard practice. More recently, following advances in technology and breast imaging, a number of different localisation methods have been described with varying results. These include: intra-operative ultrasound guided methods [4,5], haematoma-directed ultrasound guidance (HUG) [6,7], radio-guided occult lesion localisation (ROLL) [8,9] and most recently, radioactive seed localisation (RSL) [10].

RSL requires a radio-opaque titanium seed containing the radioactive isotope iodine-125 be to inserted into the centre of the tumour [10]. This localisation procedure is carried out under stereotactic or ultrasound guidance. Localisation can be performed a number of days prior to surgery, without any significant risk of seed migration [11]. During surgery, a handheld gamma probe is used to determine the location of the seed and with it, the centre point of the tumour for excision.

The RSL technique was introduced to this institution in September 2014 replacing WL as the standard procedure for localisation of non-palpable breast cancers. The primary aim of this study is to assess how this change in practice has affected the

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accuracy of tumour excision procedures. The secondary aim is to establish whether a "learning curve" for the RSL procedure could be objectively demonstrated. The primary outcome measures were inadequate margin rates and specimen weights, comparing the two localisation methods (WL and RSL). Secondary outcome measures were inadequate margin rates and specimen weights for the first hundred RSL cases compared to all subsequent RSL cases in the data set.

2. Methods

2.1. Patients& data collection

Data was collected retrospectively from the institution's histology reporting database. Patients who had undergone breast conserving surgery for a single focus of non-palpable invasive breast carcinoma were included. Pre-operative diagnosis was obtained in all cases by means of image guided core biopsy. Patients were excluded if they had in situ disease only, multifocal tumours, multiple wires/seeds for localisation, had neoadjuvant chemotherapy, or had undergone a therapeutic mammoplasty as opposed to a simple wide local excision.

The WL arm of the study was populated with the last one hundred consecutive eligible cases performed at this institution prior to changing the standard localisation method to RSL. These cases were performed between January and September 2014.All eligible cases of RSL were included from September 2014 to May 2016.

2.2. Localisation techniques

The WL cases were localised with a Reidy wire (Cook Medical, USA). The RSL cases were localised with a titanium seed containing a radioactive source of Iodine-125 (Bard Medical, USA). Wires were inserted on the morning of surgery and in the RSL cases the seed was inserted between seven and fourteen days prior to surgery. All wire and seed insertions were performed under ultrasound or stereotactic guidance by the same team of specialist breast radiologists.

2.3. Surgical excision

Surgical excision (WL and RSL) was performed by or under the direct supervision of four consultant oncoplastic breast surgeons. Surgical excision procedures were performed in exactly the same way for both groups using Level 1 oncoplastic techniques with cosmetically placed incisions (peri-areolar, infra-mammary fold or lateral skin fold). The only difference was following a wire to the site of excision or following the radioactive signal. Specimen x-ray was performed and reported on for both WL and RSL cases. Cavity margin shaves were taken when indicated by specimen x-ray or clinical suspicion of close margin.

2.4. Definitions

In this study, an *inadequate margin* is defined as presence of invasive tumour within 1 mm of an inked radial margin, where improvement of the margin is considered possible (i.e. the primary excision specimen does not extend to the anatomical perimeter of the breast, at the margin in question). At this institution, it is considered necessary to perform a re-excision of margins that are *inadequate* as per the aforementioned definition.Specimen weight is defined as the sum of the weight of the tumour specimen and the weight of any additional cavity shaves performed during the primary procedure.

2.5. Analysis

Patient demographics, tumour characteristics, specimen margin status and specimen weights were compared between the groups. Chi square test was used for categorical variables and Mann Whitney *U* test for continuous non-parametric variables. Statistical significance was considered to be $p < 0.05$.

3. Results

3.1. Primary outcomes (WL versus RSL)

A total of 333 cases were included in the study; 100 patients in the WL group and 233 in the RSL group. There were no significant differences in patient age or tumour characteristics between the two groups (Table 1). Mean age at diagnosis was 62 years in both groups. The median tumour size was 18 mm and 15 mm for WL and RSL respectively ($p = 0.14$). Histological tumour types were distributed similarly in both groups, with ductal comprising 75% (WL) and 77.2% (RSL) of cases, 7% (WL) and 11.2% (RSL) were lobular and 18% (WL) and 11.6% (RSL) were other invasive tumours (tubular, $n = 29$; papillary, $n = 7$; mucinous, $n = 7$; apocrine, $n = 1$; adenoid, $n = 1$). Modified Bloom-Richardson tumour grades had a similar distribution in both groups, with 44% and 40.8% grade I tumours, 40% and 47.2% grade II and 16% and 12% grade III (WL and RSL cases respectively). With regards to lymph node procedures, a sentinel node biopsy was performed in the vast majority of cases in both groups, with no statistically significant difference.

Pathology results pertaining to the primary outcomes are shown in Table 2. The inadequate margin rate was 18% in the WL group and 8.6% in the RSL group ($p = 0.013$) The median specimen weight was 33.3 g in the WL group compared to 28.7 g in the RSL group ($p = 0.014$).

3.2. Secondary outcomes (RSL1 versus RSL2)

The first 100 RSL cases to be performed (fulfilling inclusion criteria) constitute the RSL1 group. Subsequently, a further 133 eligible RSL procedures were performed during the study period, constituting the RSL2 group. There were no significant differences in patient age or tumour characteristics between the two groups (Table 3).

The RSL2 group had a significantly lower inadequate margin rate than that of the RSL1 group (13.0% versus 5.3%, $p = 0.037$). Fig. 1 shows the chronological distribution of cases with an inadequate margin reported, graphically demonstrating this reduction over time/experience.The median specimen weights were similar for both groups (28.6 g and 29.4 g, $p = 0.82$). These results are shown in Table 4.

3.3. Comparison of WL versus post learning curve RSL (i.e. WL versus RSL2 group)

As an objective improvement is observed within the RSL group following the first 100 cases, an analysis has been performed with the first 100 RSL cases excluded (i.e. WL versus RSL2, see Table 5). The RSL2 group had a significantly lower inadequate margin rate (18.0% versus 5.3%, $p = 0.0019$) when compared to the WL group. The median specimen weight decreased from 33.3 g in the WL group to 29.4 g in the RSL2 group ($p = 0.026$).

4. Discussion

The results of this study demonstrate that the adoption of the RSL technique (in place of WL) has resulted in a significant