Annals of Diagnostic Pathology 21 (2016) 47–52

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Comparison of margin status and lesional size between radioactive seed localized vs conventional wire localized breast lumpectomy specimens

Jason Rarick, MD [a], Bruce F. Kimler, PhD [b], Ossama Tawfik, MD, PhD [a,*]

[a] Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS, USA
[b] Department of Radiation Oncology, University of Kansas Medical Center, Kansas City, KS, USA

ARTICLE INFO

Keywords:
Breast cancer
Radioactive seeds
Conventional wire localization
Lumpectomy
Resection margins

ABSTRACT

Despite the known benefits of the use of radioactive seed localization (RSL), few studies have looked at the resultant pathologic marginal status of these lumpectomy specimens, especially in regard to different definitions of close/positive margins. We compared the marginal status of lumpectomy specimens removed by either RSL or conventional wire localization (CWL) techniques. A total of 106 lumpectomy specimens including 62 by CWL and 44 by RSL for invasive ductal and lobular carcinomas were compared. Data on gross and microscopic surgical margin status, tumor type and grade, and demographic information were retrospectively collected. There was no difference between the techniques in terms of tumor characteristics including size, histologic grade, lymph node positivity, or age. Although the distributions are very similar between CWL and RSL specimens for final marginal assessments ($P = .69$), there is a (modest) statistically significant difference in the distribution for margin classifications based on gross assessments ($P = .040$), specifically more RSL specimens exhibiting tumor within 1 mm of the closest margin. Concordance between gross and microscopic lesion measurements is highest for invasive ductal carcinoma grade 3 for both CWL and RSL lumpectomies (78.6% and 80.0%). This study shows that there were no significant marginal status differences between RSL and CWL lumpectomy specimens with invasive carcinoma. Rather, what was relevant is whether the entire specimen could be classified as having negative/close margins. Significant workflow challenges in surgical pathology laboratories are expected with the adoption of the RSL process.

1. Introduction

Breast-conserving surgical procedures predominantly highlighted by lumpectomies are becoming a popular treatment modality for breast cancer [1–3]. Decreased surgical trauma and increased aesthetics are 2 benefits using this more conservative surgical treatment choice compared with mastectomies. In addition, several studies have shown that the survival rates for these breast-conserving surgical procedures are comparable to the more extensive mastectomy surgical procedures [2–9]. Despite these benefits, one difficulty in relying on lumpectomy excisions is the higher recurrence rates in these specimens when compared with mastectomy specimens due to the more conservative surgical approach [2,3,5,6,8,9]. Many studies have shown that positive margins are associated with an increased recurrence of tumor [10–14]. Thus, complete excision of the lesion with adequate margins is of the utmost importance for lumpectomy specimens. Although complete excision of the lesion is conceptually easy to understand, the definition of adequate margins is not fully agreed upon [12–18]. In practice, there are differences between institutions and individual surgeons for what is considered an adequate margin vs a nonadequate margin that would require a reexcision or additional tissue to be removed at the time of the primary surgery. The consensus guidelines of the Society of Surgical Oncology and American Society for Radiation Oncology (SSO-ASTRO) state that tumor at ink (tumor at margin) defines a positive margin only, thus needing additional tissue to be removed [10]. Using this guideline, tumor that is close to but not touching ink would not require additional tissue submission. Studies in support of the SSO-ASTRO practice show minimal benefits from submitting additional tissue [10]. Regardless, many continue advocating the reexcision of additional tissue when there is tumor within 1 mm or 2 mm of the inked surgical margin [12–14,16–19].

Despite the controversy involved in the definition of positive and close surgical margin status, it is accepted that margin status is one of the most important prognostic factors for recurrence in invasive breast carcinomas treated by lumpectomy [12–14,20–24]. This, among others, has led to the adoption of a multidisciplinary approach where radiologists play a critical role in localizing targeted lesions for better outcomes. Conventional wire localization (CWL) immediately before surgical intervention was soon acknowledged as the new standard of care and has been used extensively for the removal of nonpalpable

* Corresponding author at: Department of Pathology and Laboratory Medicine, Kansas University Medical Center, 3901 Rainbow Blvd, Kansas City, Kansas 66160. Tel.: +1 913 588 1185; fax: +1 913 588 8780.
E-mail address: otawfik@kumc.edu (O. Tawfik).

http://dx.doi.org/10.1016/j.anndiagpath.2016.01.003
1092-9134/

lesions in the lumpectomy specimen in its entirety in an attempt to obtain negative margins [15,25–28]. Because of the many limitations of the wire localization procedure, many institutions including ours have adopted the radioactive seed localization (RSL) as an acceptable alternative [29–36]. The latter is aided by the use of imaging tools for scanning lumpectomy specimens, both whole and after slicing, so that the targeted lesion and intraoperative margin status can be obtained [29–36].

Few studies have looked at the resultant pathologic margin status of these lumpectomy specimens using RSL with the Faxitron scanning system compared with CWL lumpectomy gross margin status [34–37]. The goal of this work was to analyze the margin status of CWL and RSL lumpectomy specimens, especially noting the differences between intraoperative gross measurements vs the more precise and conclusive microscopic measurements for both groups. In particular, we wanted to see if the compact localized nature of RSL lumpectomy specimens allows for more complete excisions of breast cancer cases with reduced positive/close margins. In addition, as a surrogate of the possible benefits of using RSL lumpectomies with intraoperative imaging, we also studied the impact of gross to microscopic tumor size for CWL and RSL groups of lumpectomy specimens as well as the effect of histologic type and grade of tumors.

2. Materials and methods

This retrospective study was approved by the institutional review committee at the University of Kansas Medical Center. A retrospective review was performed of all lumpectomy specimens at our institution that were positive for invasive carcinoma over a 1-year period: January, 1, 2014, to January 13, 2015. Data collected included the use of either CWL or RSL, gross margin status, microscopic margin status, gross lesion dimensions, microscopic lesion dimensions, histologic diagnosis, and if there was prior neoadjuvant chemotherapy. In addition, the histologic grade of the invasive carcinomas was noted. Lumpectomy specimens that contained more than 1 focus of invasive carcinoma were excluded from the study, along with invasive carcinomas that were not conventional invasive ductal (IDC) or invasive lobular carcinomas (ILC).

A total of 106 lumpectomy cases were obtained for the margin analysis study; all cases were diagnosed as either IDC or ILC. A total of 62 CWL lumpectomies and 44 RSL lumpectomies were reviewed. All tumors were graded using the modified "Nottingham" criteria of Bloom and Richardson [38]. Conventional wire localized lumpectomy tumors included 13 IDCs grade 1, 21 IDCs grade 2, 14 IDCs grade 3, and 14 ILCs grades 1 and 2 combined. The seed localized tumors included 8 IDCs grade 1, 21 IDCs grade 2, 6 IDCs grade 3, and 9 ILC tumors grades 1 and 2 combined. Most of the ILCs were grade 2; accordingly, all ILCs were combined together because of the small total number of grade 1 ILCs with no grade 3 cases for both CWL and RSL cases.

The gross and microscopic marginal status for both CWL and RSL lumpectomy specimens was collected for all 6 surface areas, including anterior, posterior, superior, inferior, lateral, and medial margins for each lumpectomy specimen. For both gross and microscopic assessments, distance to tumor (invasive or ductal carcinoma in situ or both) was estimated with 1-mm precision. Margins greater than 5 mm were recorded simply as 5 mm. *Close margins* are defined as either invasive or ductal carcinoma in situ, or both present either within 1 mm or within 2 mm from the inked margin. *Positive margins* are defined as tumor present at the inked margin.

Concordance and variance were then evaluated between the microscopic and gross margin measurements for each dimension for each lumpectomy specimen. The variance for each measurement was measured by subtracting the gross margin measurement by the final microscopic measurement. Concordant margins are margins where this value is 0, or in other words, the gross margin is the same as the microscopic margins (1-mm resolution). Gross overestimation of the margin was defined as a positive value, a gross margin that is larger than the final microscopic margin. Gross underestimation of the margin was defined as a negative value, a gross margin that is smaller than the final microscopic margin. The frequency of concordance, gross overestimation, and gross underestimation was compared between CWL and RSL lumpectomy specimens.

We also examined the impact of differences in gross/intraoperative tumor size in comparison with the tumor size following microscopic evaluation and the marginal status of CWL and RSL lumpectomy specimens. *Lesional size* was defined as the largest tumor dimension both grossly and microscopically. The gross and microscopic tumor size concordance was then recorded for each lumpectomy specimen. Gross over- or underestimation of lesional size was defined as a positive or negative value as compared with the actual lesional size as evaluated microscopically. The percentage of concordance of gross over- or underestimation was noted for both CWL and RSL lumpectomy specimens. Data were also analyzed according to the diagnosis of invasive carcinoma and histologic grade.

2.1. Statistical analysis

The concordance between gross and microscopic measurements of all 6 margins in all lumpectomy resection specimens was compared by Mann-Whitney nonparametric test. Assessment of concordance or discordance between gross and microscopic measurements within groups was evaluated by Wilcoxon signed rank test. Finally, the Fisher exact test was used to evaluate the final margin characterization using all 6 margins to define minimal margin, with comparison between CWL and RSL lumpectomy specimens. No corrections were made for multiple comparisons.

3. Results

The Figure (A and B) shows representative examples of wire and seed localized breast lumpectomy specimens. Table 1 highlights the distribution of clinical and histopathologic parameters of patients undergoing wire and seed localized lumpectomy. Patients that received CWL were slightly older than those that received RSL (median age of 65 vs 61 years), but this was not statistically significant. The median tumor size of patients in both groups was identical (1.2 cm). The overall majority of the tumors were of the ductal type (78%). Fifty-one percent of the IDC cases were grade II, whereas the majority of the ILC cases were grade II (70%). As expected, a large number of the lumpectomy specimens were accompanied by sentinel node biopsies, the majority of which were free of metastasis (80%) (Table 1).

Table 2 provides the distribution of intervals between resection surface and tumor for all 636 surface faces. The distance from surface to tumor was at least 5 mm for the majority of surfaces; with 81% for CWL specimens and 79% for RSL specimens by gross assessment and 72% for CWL specimens and 75% for RSL specimens by microscopic assessment. Despite this, anterior and posterior surfaces from CWL specimens assessed grossly or microscopically exhibited greater margins than RSL specimens. Conversely, superior surfaces assessed microscopically showed lesser margins for CWL specimens than for RSL specimens ($P < .017$).

Table 3 shows the concordance between gross and microscopic measurements of all 636 lumpectomy resection surfaces (6 surfaces for each of 106 specimens). Overall, 74% of margins show concordance, with no difference between CWL specimens (72%) and RSL specimens (76%) when compared by Mann-Whitney nonparametric test. Although there are almost twice as many overestimations as underestimations overall (108 vs 58; $P < .001$), this is driven entirely by the CWL specimens (71 vs 32; $P < .001$) with no significant difference ($P = .26$) between gross and microscopic margins for RSL specimens. When comparing the absolute difference of margins derived from gross and microscopic measurements, there is no difference between CWL and RSL specimens (rightmost column). When a minimum margin is