Title: Accuracy assessment methods of tissue marker clip placement after 11-gauge vacuum-assisted stereotactic breast biopsy: comparison of measurements using direct and conventional methods

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Abstract

Background: The objective of the study was to compare direct measurement with a conventional method for evaluation of clip placement in stereotactic vacuum-assisted breast biopsy (ST-VAB) and to evaluate the accuracy of clip placement using the direct method.

Methods: Accuracy of clip placement was assessed by measuring the distance from a residual calcification of a targeted calcification cluster to a clip on a mammogram after ST-VAB. Distances in the craniocaudal (CC) and mediolateral oblique (MLO) views were measured in 28 subjects with mammograms recorded twice or more after ST-VAB. The difference in the distance between the first and second measurements was defined as the reproducibility and was compared with that from a conventional method using a mask system with overlap of transparent film on the mammogram. The 3D clip-to-calcification distance was measured using the direct method in 71 subjects.

Results: The reproducibility of the direct method was higher than that of the conventional method in CC and MLO views ($P=0.002$, $P<0.001$). The median 3D clip-to-calcification distance was 2.8 mm, with an interquartile range of 2.0–4.8 mm and a range of 1.1–36.3 mm.

Conclusion: The direct method used in this study was more accurate than the conventional method, and gave a median 3D distance of 2.8 mm between the calcification and clip.

Introduction

Vacuum-assisted breast biopsy (VAB) was introduced in 1995 and is more accurate than core needle biopsy (CNB) for diagnosis of breast cancer [1–3]. Stereotactic VAB (ST-VAB) is performed to find non-palpable calcified lesions that are difficult to detect with ultrasonic images and to differentiate benign and malignant lesions imaged in a mammogram. ST-VAB has sensitivity ≥99% [4] and specificity of 100% [5], and is widely used for histological examination in surgical biopsy because of its safety and reliability.

ST-VAB with an 11-gauge probe can provide tissue of approximately 100 mg/sample and remove abnormal regions detected on mammography with a maximum diameter of 25 mm, which allows complete resection of samples for differentiation of benign or malignant calcification [6–8]. However, lesions remain in 70–73% of cases and require surgical resection [6,8]. For a patient in whom all calcifications are removed, placement of a tissue clip is used to mark the sampling point. If sample tissues are malignant, breast-conserving surgery focusing on the clip is subsequently performed. Even if sample tissues are benign, the patient is usually followed up for a certain period with a focus on the clip. Therefore, the clip must be placed accurately at the biopsy site.

Several studies have examined the accuracy of clip placement [9–11]. Placement accuracy was evaluated using a mammogram after ST-VAB in subjects including patients in whom targeted calcifications could and could not be completely removed. In those with complete resection of targeted calcifications, the resection point was estimated and the distance from the point to the clip was measured. However, mammography cannot image at exactly the same position every time, and calcifications and a clip in a mammogram are not displayed at the same point [12]. Therefore, estimation of the position at which targeted calcifications were removed using a mammogram and measurement of the target-to-clip distance may not be accurate. New tissue markers [13,14] have recently been used in mammograms and sonogram and these may increase the clip placement accuracy. Therefore, it is necessary to develop a new method for accurate measurement.

In this study, the accuracy of clip placement was measured in patients with clustered calcification in whom residual calcification was detected after ST-VAB. The distance from the residual calcification to the clip was directly measured in all subjects. The reproducibility of direct measurement was compared with that in conventional measurement. The three-dimensional (3D) distance from the calcification to the clip was also estimated using direct measurement and the accuracy of clip placement was evaluated.

The objectives of the study were to compare direct and conventional measurements for evaluation of clip placement in ST-VAB and to evaluate the accuracy of clip placement using the direct measurement method.

Materials and Methods

Subjects

This study was approved by the institutional ethics committee. Informed consent was not required for use of medical information and images. However, all patients provided written informed consent to undergo ST-VAB. The subjects were 330 consecutive patients (Table) who underwent ST-VAB in a public hospital in Osaka, Japan, from January 1, 2008 to December 31, 2013. Targeted calcifications were collected in 323 of the 330 subjects. In 7 subjects (2.2%) the procedure was considered unsuccessful because calcification was extremely light or could not be collected due to a lag in the tested position of calcification.

ST-VAB

ST-VAB was performed by one radiologist and one of two breast surgeons (ST-VAB experience: beginner, and 3 and 5 y) using a prone-positioning operating table with digital imaging (MultiCare Platinum: Hologic, Bedford, MA, USA) and an aspirator (Mammotome® System Control Module: Plexus Electronic Assembly, Neenah, WI, USA) with an 11-gauge probe (11G or 11GB Mammotome® ST Probe: Devicor Medical Product, Tijuana, Mexico). Standard techniques in the user manual were used, except that 3 tissue samples were collected. Radiography was performed to detect the targeted calcification. If samples were insufficient, a further 3 samples were collected and radiography was performed again. This procedure was continued until calcification was detected by radiography. If calcification was not found, the examination was completed and the procedure was considered to be unsuccessful.

Clip placement

A clip (Micromark®II Tissue Marker: Devicor Medical Products) was placed in subjects with small lesions in whom target calcifications were small and all were fully collected. The probe was pulled back 5 mm to position the end of the ramp of the outer catheter at the collection point, and then the clip was placed. Clip placement was confirmed by radiography before opening the pressure paddle.

Mammography

Subjects with clip placement underwent mammography in craniocaudal (CC), mediolateral oblique (MLO) and magnified mediolateral (ML) views before ST-VAB and during follow-up. Mammography was conducted using one of three devices (M-IV, Hitachi Medical, Tokyo, Japan; MGS, Toshiba Medical, Tokyo, Japan; and AMULET

Innovality, FujiFilm Medical, Tokyo, Japan) in accordance with Japanese mammography guidelines [15]. Two devices (M-IV, MGS) use a computed radiography system (Profect CS; FujiFilm Medical) and the read-out and write-in were 50 μm. The AMULET Innovality has a FPD system (50 μm). Mammography was conducted by 6 mammographers certified by the Japan Central Organization on Quality Assurance in Breast Cancer Screening [16].

Assessment of accuracy of clip placement

Mask [9] and superimposition [10,11] systems are used in conventional methods. The mask system uses overlap of a transparent film on the mammogram before ST-VAB, and the nipple, skin and targeted calcifications are plotted with a marker pen. The film is then overlapped on the mammogram after ST-VAB to measure the distance from the clip on the mammogram to calcifications on the film (Figs. 1a,b). This measurement was performed on mammograms in CC and MLO views. The superimposition method determines the positions of clips and lesions by aligning mammograms before and after biopsy using landmarks (e.g. nipple, pectoralis, and vasculature) of mammary parenchyma and soft tissues.

In the direct method used in this study, the distance from a clip to residuals of targeted lesions in ST-VAB is measured directly. Therefore, the subjects were patients with targeted cluster calcifications in whom a clip was placed in ST-VAB. Residuals of targeted cluster calcifications were confirmed on mammograms in CC and ML views after ST-VAB to allow direct measurement of the clip-to-residual calcification distance. The distance measured was from the center of a clip with a 2-mm diameter to the nearest residual calcification (Fig. 2a).

Comparison of conventional and direct methods

The reproducibility of the clip-to-calcification distance on mammography was examined to evaluate the utility of the direct method compared with the conventional method. A mask system was used as the conventional method based on superimposition of landmarks of mammary parenchyma and soft tissues. The clip-to-calcification distance was measured on the mammogram after ST-VAB and on a mammogram taken on another day. The difference in these distances was used to evaluate the reproducibility. These measurements required targeted calcifications visible on mammograms in CC and MLO views before ST-VAB and residual calcifications and clips visible on mammograms in CC and MLO views taken twice after ST-VAB (Fig. 3). These criteria were met by 28 subjects (Table). The methods of assessment of reproducibility for the conventional and direct methods are shown in Figs. 1c,d and 2a,b, respectively. Reproducibility was estimated in CC and MLO views.

The reproducibility of the conventional method was determined with transparent films overlapped on mammograms displayed in full size on a 5M pixel thin-film transistor liquid crystal display (TFT-LCD, RadiForce RX340: EIZO Corp., Ishikawa, Japan), using mammography viewer software (Synapse EX-V: Fujifilm Medical). The clip-to-calcification distance on translucent films was measured with a ruler. In the reproducibility of the direct method, the clip-to-calcification distance was measured using a distance tool on the software. The reproducibilities of the two methods were measured on the same mammogram and in CC and MLO views (Fig. 2) by 3 mammographers who were certified as above [16].

Assessment of accuracy of clip placement using the direct method

Assessment of the accuracy of clip placement using the direct method required that targeted residual calcifications and clips were visible on one mammogram in CC and magnified ML views after ST-VAB (Fig. 3). These criteria were met by 71 subjects (Table). Coordinates of clips from calcifications were (x_0, z_1) on CC views and (y_0, z_2) on magnified ML views. The 3D distance was estimated using the Pythagorean theorem

(Fig. 4). Since z_1 on the CC view and z_2 on the magnified ML view were inconsistent with each other, the mean of these coordinates was used. Measurements were performed by three technicians for comparison of the conventional and direct methods, and median values were used in the analysis.

Statistical analysis

The difference in reproducibility between the conventional and direct methods was examined using a generalized linear model (GLM) for repeated measures. If results differed between measurers, the difference between the two methods cannot be examined without accounting for measurer differences. Therefore, the significance of differences between measurers was examined. The homogeneity of analysis of variance (ANOVA) was examined by Mauchly's sphericity test and the significance of intersection was determined under the assumption of sphericity if homogeneity was confirmed and by Greenhouse-Geisser correction if homogeneity was not confirmed. The accuracy of clip placement using the direct method for 3 measurers was examined using intraclass correlation coefficients (ICCs). The significance level was set at 0.05 and all analyses were performed using SPSS (Statistics Base ver. 23.0; IBM, Armonk, NY, USA).

Results

Comparison of conventional and direct measurements

There was no significant difference in reproducibility between measurers in the CC view for the conventional and direct methods (between measurers: P=0.622, between measurers and methods: 0.937), confirming the homogeneity of ANOVA. The significance of intersection was examined under the assumption of sphericity, but again there was no significant difference between measurers (P=0.078). Therefore, comparison of the conventional and direct methods was performed in the CC view without considering the effects of measurers. A comparison of reproducibility of the two methods in CC views is shown in Fig. 5. The reproducibility of the direct method was significantly higher than that of the conventional method (P=0.002, 95% confidence interval (CI): 0.72–2.78). Mauchly's sphericity test also showed no significant difference in the MLO view (between measurers: P=0.65, between measurers and methods: 0.32), showing the homogeneity of ANOVA, and there was also no significant intersection between measurers (P=0.079). Therefore, the conventional and direct methods in the MLO view were also compared without considering the effects of measurers. The comparison in Fig. 6 indicates significantly higher reproducibility of the direct method compared to the conventional method in the MLO view (P<0.001, 95% CI: 1.18–2.93).

Accuracy of clip placement using direct measurement

Examination of the reliability among three measurers gave a ratio of variance of F=2.63 and p=0.075 without differences between measurers (ICC (2,1)=0.96). This indicates high reliability [17]. The median 3D calcification-to-clip distance was 2.8 mm, the interquartile range was 2.0–4.8 mm, and the range was 1.1–36.3 mm. This distance was <5 mm in 55 subjects (78%), ≥5 to <10 mm in 12 (17%), ≥10 to <20 mm in 2 (0.03%), ≥20 to <30 mm in 0, and ≥30 to <40 mm in 2 (0.03%) (Fig. 7).

Discussion

Previous studies of the accuracy of clip placement in ST-VAB have included patients with and without residual calcification on mammograms. Cases without residual calcification were assessed based on the estimated site of calcification. A new method was used in this study in patients with residual calcification, in which the distance from the calcification to the clip was measured directly. The accuracy of this method was higher than that of the conventional method. The accuracy of clip placement was also assessed by determination of the 3D calcification-to-clip distance using the direct measurement method.

Mask [9] and superimposed [11] measurement systems have been used for assessment of clip placement, but these systems have limited accuracy due to differences in breast shapes in different mammograms [9]. Consequently, calcifications and clips are not visualized at the same point [12] and it is difficult to overlap a calcification and a clip in different mammograms or to align them visually. Several studies have reported direct measurement of the distance from a clip to a residual calcification and hematoma. Uematsu et al. [10] measured distances from a clip to a residual calcification, cavity or hematoma in patients with visible lesions on mammograms, but superimposition was used for patients without visible lesions

(28/204). Rosen et al. [11] directly measured distances from the center of a cavity or hematoma or central lesion to a clip using a mask system in patients with visible lesions on mammograms, but again superimposition was required for patients without visible lesions. Thus, direct measurement was not used in all subjects, but mask and superimposition systems were combined with direct measurement. In addition, the procedure for determining the center was not described, and this may have influenced the results. The results of this study showed that the direct method had significantly higher reproducibility than the conventional method. Direct measurement in all subjects makes assessment more accurate. Assessment of clip placement was conducted only in subjects for whom direct measurement was available and the distance was determined from a clip to the residual calcification nearest to the clip. This measurement is not from the center of the sampling site, but the size of the cluster calcification was limited, giving a more objective measurement than estimation of the lesion center.

The accuracy of clip placement was assessed by the 3D distance using the direct method. Previous studies have assessed accuracy separately in different 2D mammograms, and may have underestimated the accuracy [11]. In this study, the longest distance was assessed by estimating the 3D clip-to-calcification distance, thereby avoiding underestimation due to 2D distance measurement. The clip-to-calcification distance was determined directly, making it unlikely to be affected by positioning compared with a conventional measurement, but this effect is not completely eliminated. However, 3D measurement reduces the effect of positioning in comparison with a 1D assessment. Few studies have determined the accuracy of clip placement using a 3D distance. Liberman et al. [18] and Reynolds et al. [19] examined x, y and z coordinates in lesions and clips and measured the lesion-to-clip distance. Coordinates of the target and clip were determined while pressing the breast with a compression paddle, followed by measurement of 3D positions and estimation of the distance during ST-VAB. However, clips may move in the direction of the compression paddle [10,11,20]. Kass et al. [21] measured 3D distances on mammograms in CC and ML views, with adjustment of the distance from the MLO view using a cosine function for subjects without an ML view. However, the measurement system itself was unclear in this study.

Previous studies of the accuracy of clip placement have included subjects with and without residual calcifications and hematoma. To our knowledge, no study has been performed in subjects limited to those with residual calcification found after biopsy. Since 3D distance was measured for assessment in this study, the clip position was accurately assessed. The median clip-to-calcification distance was 2.8 mm and the clip was placed less than 10 mm from the calcification in 67 of 71 subjects (95%). Given that the window width of a probe is 19.4 mm, this placement accuracy is very high. The median number of collected samples was low (3 per ST-VAB) and there were few hematomas and cavities after biopsy; therefore, the clip caught tissues, leading to a high accuracy of clip placement. However, Uematsu et al. [10] found that the number of samples per biopsy was not related to a lag in clip placement, for reasons that are unclear. The clip-lesion distance may be underestimated in conventional methods [11], but the 3D distance in this study showed less misalignment of the clip and lesion. This suggests lower reproducibility of the conventional method compared to the direct method, resulting in overestimation, rather than underestimation, of the clip-lesion distance.

Two subjects had a lag beyond 24 mm between the clip placement and sampling positions [9], which was defined as clinically serious in this study. The lags were 31.9 and 36.3 mm, respectively, and these distances indicate clip wandering. This could be due to an accordion effect, clip wandering in a biopsy track, clip floating due to a hematoma, clip replacement by a hematoma, and a changed clip site due to air absorption in a biopsy cavity [20]. Clip wandering is also frequently found in thin breasts [10]. Placement of two clips [20] and comparison with the mammogram before sampling may reduce this problem. However, comparison with a mammogram before sampling is ineffective without residual calcification, and the efficacy of placement of two clips has not been widely examined.

A decision on clip placement is generally made for follow-up of sampling sites when all cluster calcifications in a biopsy are collected. However, in this study, clips were placed in all subjects with small lesions in whom a targeted cluster calcification could be fully collected. Therefore, clips were placed in a residual calcification of a cluster calcification. This was to determine the resection range under C-arm diaphanoscopy using a clip as the marker, in order to minimize the resection range of a limited lesion if biopsy tissues were malignant [22].

This study had several limitations. First, the mean of z_1 and z_2 was used for z in calculation of the 3D distance for assessment of the accuracy of clip placement because z_1 on the CC view and z_2 on the magnified ML view were inconsistent. This inconsistency was not due to the ML view using a magnified image and the CC view using a standard image, since the actual distance in the magnified image can be determined using a tool for distance measurement. The inconsistency was caused by visualization of the CC and magnified ML views in different directions and different view positioning. However, direct measurement was used in this study and the effect of positioning is relatively unimportant. Second, reproducibility of measurements was assessed in only 28 subjects because there were few patients who underwent ST-VAB who met the inclusion criteria for reproducibility assessment. Accumulation of subjects who meet the criteria for assessment of the accuracy of clip placement using direct measurement is required. Of 330 patients in our hospital, only 71 met the inclusion criteria, and thus studies at hospitals with many ST-VAB procedures are needed.

Tissue markers visualized in mammograms and by breast ultrasonography give high placement accuracy, but wandering also occurs [13,14]. The lag between markers and collection sites is a concern [13] and placement accuracy has not been widely studied. The direct method used in this study provides more accurate assessment of marker positions.

Conclusions

The accuracy of a direct method for assessment of clip placement in ST-VAB was significantly higher than that of the conventional method. The median clip-to-calcification distance using the direct method was 2.8 mm and the range was 1.1 to 36.3 mm.

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