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# Real-Time 3-Dimensional Virtual Reality Navigation System with Open MRI for Breast-Conserving Surgery

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- BACKGROUND:** The aim of this study was to report on the early experiences using a real-time 3-dimensional (3D) virtual reality navigation system with open MRI for breast-conserving surgery.
- STUDY DESIGN:** We developed a real-time 3D virtual reality navigation system with open MRI, and evaluated the mismatch between the navigation system and real distance using a 3D phantom. Two patients with nonpalpable MRI-detected breast tumors underwent breast-conserving surgery under the guidance of the navigation system. An initial MRI for the breast tumor using skin-affixed markers was performed immediately before excision. A percutaneous intramammary dye marker was applied to delineate an excision line, and the computer software “3D Slicer” generated a real-time 3D virtual reality model of the tumor and the puncture needle in the breast. Excision of the tumor was performed in the usual manner along the excision line indicated with the dye. The resected specimens were carefully examined histopathologically.
- RESULTS:** The mean mismatch between the navigation system and real distance was  $2.01 \pm 0.32$  mm when evaluated with the 3D phantom. Under guidance by the navigation system, a percutaneous intramammary dye marker was applied without any difficulty. Fiducial registration errors were 3.00 mm for patient no. 1, and 4.07 mm for patient no. 2. Histopathological examinations of the resected specimens of the 2 patients showed noninvasive ductal carcinoma in situ. The surgical margins were free of carcinoma cells.
- CONCLUSIONS:** Real-time 3D virtual reality navigation system with open MRI is feasible for safe and accurate excision of nonpalpable MRI-detected breast tumors. Long-term outcomes of this technique should be evaluated further. (J Am Coll Surg 2010;210:927–933. © 2010 by the American College of Surgeons)
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Achieving sufficient surgical margins when excising breast tumors by breast-conserving surgery (BCS) might not be achievable when the tumor is nonpalpable and the extent of

the tumor is difficult to evaluate using mammography or ultrasonography.

Ductal carcinoma in situ (DCIS) is a typical nonpalpable breast cancer that has been classified as an image-detected breast cancer.<sup>1</sup> Recently, MRI was confirmed to be clinically important in the diagnosis of DCIS.<sup>2</sup> Breast MRI might be an ideal modality for image-guided surgery for DCIS, and it is expected that surgical treatment will be combined with MRI in the future.<sup>3</sup>

At Kyushu University Hospital (Fukuoka, Japan), an open MRI therapeutic room was established in 2005.<sup>4</sup> This room is equipped with MR-compatible instruments, such as a surgical bed, ventilator, and vitals-monitoring system, so that procedures such as abdominal surgery with open laparotomy can be performed under general anesthesia. Using the open MRI therapeutic room, we developed a real-time 3-dimensional (3D) virtual reality navigation system designed for percutaneous abdominal interventions,<sup>5</sup>

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**Abbreviations and Acronyms**

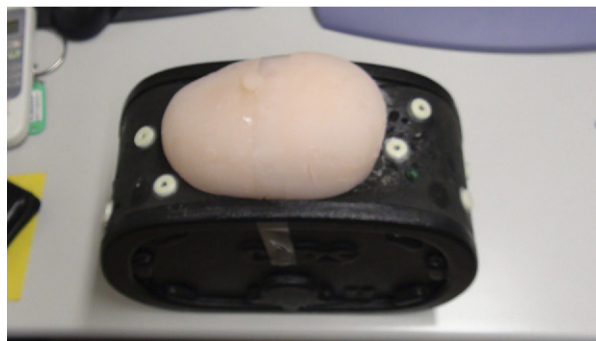
BCS	= breast-conserving surgery
3D	= 3-dimensional
DCIS	= ductal carcinoma in situ
FRE	= fiducial registration error

with the intention of applying the navigation system to other interventions in the future. After a pilot study was carried out to assess the system when applied to BCS, we successfully performed BCS on 2 DCIS cases, such that sufficient surgical margins were achieved when accurately delineated by intramammary dye marking under the guidance of the navigation system. Here we report on our early experiences with the navigation system and evaluate the feasibility of using this navigation system for BCS.

**METHODS****A pilot study**

To assess the proposed system, quantitative and qualitative evaluations were carried out in a pilot study using a 3D phantom. The quantitative evaluation criteria were the accuracy of needle insertion and the time required to complete the insertion into the target. The qualitative evaluation criterion was the usefulness of the navigation system according to the surgeons' opinions, which was assigned using a qualitative grading scale.

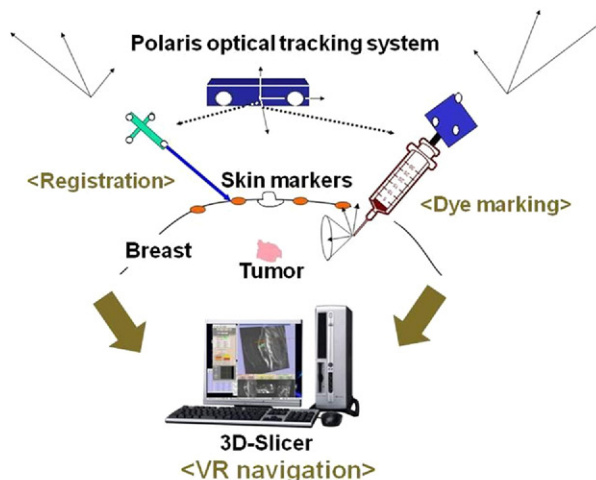
A commercial multimodality interventional 3D mammary phantom (BB-01, OST Co. Ltd.) was used (Fig. 1A). Four tumor models approximately 6 mm in diameter (Breathcare; Kobayashi Pharmaceutical Co. Ltd) were incorporated into the phantom. Among them, we selected 2 tumors that could be clearly identified by MRI within the phantom. Two surgeons with 11 and 20 years clinical experience performed the insertions into 2 identical tumor models. For each target, the surgeons performed the insertions into 4 sites, which were 2 cm away from the tumor as indicated by the navigation system, and an intramammary dye marking was performed (Figs. 1B, 1C). In phantom experiments, it was found that when the number of insertion sites was  $\geq 5$ , the dye distribution at each injected site sometimes overlapped, making it difficult to distinguish 1 injection site from another. As a result, the number of insertion sites was limited to 4, and the sites were located in a cross direction 2 cm away from the tumor, as indicated by the navigation system. To evaluate the accuracy of the marking procedure, we evaluated the dye distribution in the phantom and measured the real distance between the tumor model and the injection site, and analyzed the mismatch between the distance, indicated by the navigation



A



B



C

**Figure 1.** (A) The 3-dimensional mammary phantom with skin markers used in the pilot study. The 4 tumor models approximately 6 mm in diameter were incorporated in the phantom. (B) A surgeon is performing the insertions into a tumor model indicated by the navigation system to make an intramammary dye marking. (C) Overview of the navigation system: the acquired MR images and the patient coordinates were integrated using a customized version of the freely available navigation software, 3D Slicer.

**Table 1.** Demographic Data

Patient no.	Age (y)/gender	Chief symptom	Tumor palpation	Preoperative diagnosis
1	59/F	Bloody nipple discharge of the left breast	No	DCIS, left
2	55/F	None (detected with medical check)	No	DCIS, left

DCIS, ductal carcinoma in situ; F, female.

system and the real distance. The time required to complete the insertion into the target by each of the 2 surgeons was measured. The surgeons' opinions about the usefulness of the navigation system were expressed by assigning a grade of 1, not useful; 2, slightly useful; 3, normally useful; 4, very useful; or 5, extremely useful.

### Patients

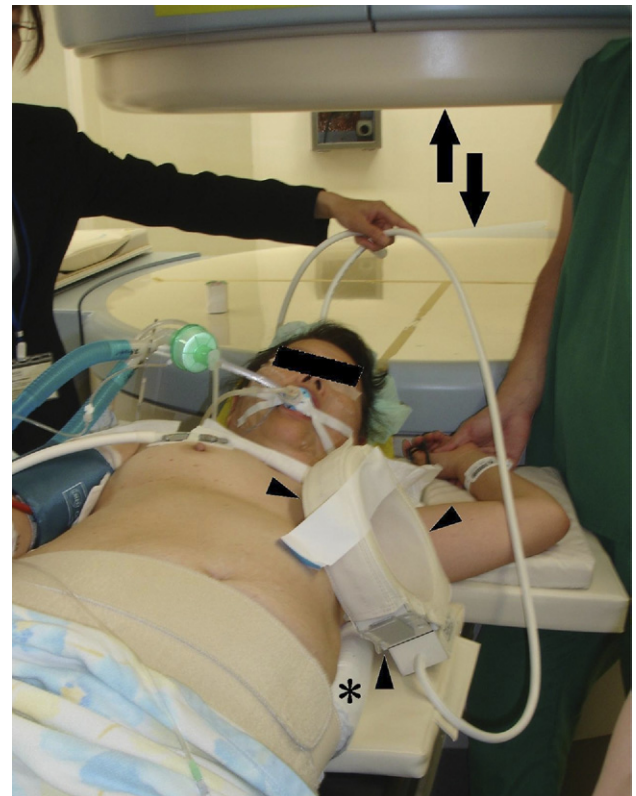
Table 1 indicates the demographic data of both patients. Tumor extent was difficult to evaluate using mammography and ultrasonography, although when using mammography diffuse calcifications could be localized in both patients. A high magnetic field closed-bore MRI clearly revealed the extent of the tumors in both patients. DCIS was highly suspected as a diagnosis in both patients. Therefore, BCS was scheduled to enable a definitive diagnosis and effective treatment.

Written informed consent was obtained from each patient after a full explanation of the purpose, nature, and risks of all procedures. The institutional review board of Kyushu University Hospital approved all study procedures.

### Dye marking under guidance of real-time 3D virtual reality navigation

All procedures were performed in the open MRI therapeutic room. First, the patient was placed in the supine position and general anesthesia was applied. The patient was then moved to the left "surgical position," that is, the same position that would be used for the procedure, and the arm on the affected side of the patient was placed on the table above the patient's head; the patient was then fixed in the supine oblique position using an oblique board placed at an angle of 10 degrees<sup>6</sup> (Fig. 2). After 6 to 9 skin-affixed multimodality markers (IZI Medical Products Inc.) were affixed to the patient's breast, an initial MRI scan was performed using a 0.4-T open MRI (Aperto; Hitachi Medical Co.) to image the breast tumor and skin markers. The patient was then moved out of the MR gantry and paired point registration was performed. The registration between the patient and the MR images was done using the Polaris optical tracking system (NDI), and involves a matching process between the patient and MR image coordinate systems. The Polaris-based coordinate of each skin-affixed multimodality marker on the patient's breast was obtained by identifying each marker using a probe that reflects in-

frared light (Fig. 1C). The acquired MR images and patient coordinates were integrated using a customized version of freely available navigation software (3D Slicer, developed by the Artificial Intelligence Laboratory of the Massachusetts Institute of Technology and by Brigham & Women's Hospital, a teaching affiliate of Harvard Medical School).<sup>7</sup> The infrared light-reflecting markers were attached to a syringe and puncture needle and, using the 3D-Slicer software, connected to the Polaris system, and real-time virtual reality images were generated that reflected the needle movements (Fig. 1C). A dye (indigotindisulfonate sodium) was loaded into the marker-equipped syringe. During percutaneous intramammary dye marking to delineate the dissection line of the tumor, the 3D-Slicer generated a real-



**Figure 2.** An initial MR image scan was performed in our open MRI therapeutic room before excision to image a breast tumor with the patient under general transtracheal anesthesia. The patient was fixed in the surgical position using an oblique board (\*), and bandages. Note the MR-coil (arrowheads) is placed on the breast and the open MRI is located in the back (arrows).



**Figure 3.** Left, percutaneous intramammary injection of dye in the syringe to make a dissection line of the tumor with the navigation of 3D Slicer. Arrowheads, skin markers; asterisk, a syringe attached with infrared markers; right, virtual MR images on the monitor of 3D Slicer reflecting the same slice as the puncture line. A breast tumor is indicated in green; a needle and a puncture line are indicated in red.

time 3D virtual model of the tumor, puncture needle, and puncture line in the patient's breast (Fig. 3). The virtual tumor model represents the tumor as a polyhedron that consists of a number of polygons. The number of polygons necessary to model the tumor varies, depending on the size and decimation parameter. Injection sites were chosen circumferentially 2 cm apart from the horizontal edge of the tumor and at the same depth as the center of the tumor vertically, as the tumors are usually excised with a 2-cm surgical margin when performing BCS at our institution. The number of injection sites depended on both the surgeon's intention and the tumor morphology, however, the distance between sites was usually about 5 mm.

The fiducial registration error (FRE) is the root mean square error between the original marker positions and the transformed marker positions in the MR images. When the coordinates of the markers are presented in a random order, the FRE is computed and the best pair matching that produced the minimum FRE is determined automatically.

A 3D volume-rendered image was constructed from the MR volume data using an image analysis workstation (Virtual Place Raijin; AZE), and was used to assist in the evaluation of the navigation system.

### Excision of the tumor and examination of the resected specimens

Thereafter, excision of the tumor was performed in the usual manner along the dissection line indicated by the dye marking. Immediately after excision, an MRI scan was performed again to evaluate the excised area. Before completing the operation, the calcifications present in the resected specimen were estimated using a specimen mammography.

Postoperative patient care was carried out according to our institution's standard protocol. The resected specimens were carefully examined macroscopically and were sliced into contiguous 5-mm sections. Histopathological examinations were performed by a pathologist and were used to evaluate the surgical margin using hematoxylin-eosin staining.

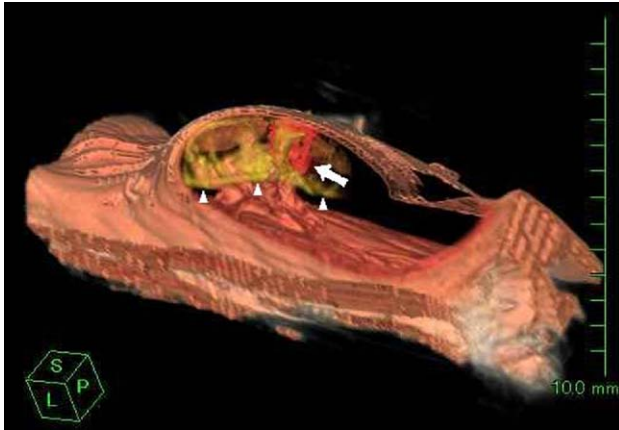
## RESULTS

### A pilot study

Mean distance between the tumor model and the injection site was 2.01 mm, with a standard deviation of 0.32 mm. Time required to complete the insertion into the target was 25 seconds, with a standard deviation of 3.5 seconds, for 1 surgeon with 20 years clinical experience; and 32 seconds, with a standard deviation of 10.2 seconds, for a 2<sup>nd</sup> surgeon with 11 years clinical experience. Both surgeons assigned a score of grade 4 when qualitatively evaluating the navigation system's use. Therefore, it was concluded that the navigation system was very useful in the opinion of the surgeons using the system.

### Operative outcomes with real-time 3D virtual reality navigation system

During the operations on the DCIS patients, the customized 3D-Slicer software clearly showed virtual reality images on the monitor in real-time, including the position, direction, and movements of the puncture needle and the tumor. In this clinical study, approximately 300 to 400 polygons were used to construct the virtual tumor polyhedron model, and this was found to be sufficient to accurately delineate the tumors.



**Figure 4.** Immediately after marking, a 3-dimensional volume-rendered image constructed from the MR volume data using Virtual Place Raijin clearly showed the dissection line with interrupted dye marking encircling the tumor. Arrow (red), a breast tumor; arrow heads (yellow), dye distribution.

Percutaneous intramammary injection of the marker dye was performed without any difficulty under the guidance of the navigation system. Time required to complete the dye marking around the tumors was approximately 14 minutes for patient no. 1 and 26 minutes for patient no. 2.

The FRE was 3.00 mm for patient no. 1 and 4.07 mm for patient no. 2. A 3D volume-rendered image constructed from the MR volume data acquired immediately after marking clearly showed the dissection line with interrupted dye marking around the tumor (Fig. 4).

During the excisions, no complications or other difficulties occurred. A 3D volume-rendered image constructed from the MR volume data acquired immediately after the excision clearly showed the excised area that had contained the tumor. A mammogram of each specimen was acquired before completing the operation, and was confirmed to include all calcifications identified preoperatively. Postoperative outcomes for both patients were excellent and both patients were discharged from our hospital 2 days after the operation.

A histopathological examination of the resected specimen from patient no. 1 showed noninvasive DCIS. The clusters of carcinoma cells were observed in some dilated mammary ducts. The surgical margins were free of carcinoma cells. The histopathological examination of the resected specimen from patient no. 2 showed noninvasive ductal carcinoma that had proliferated within the mammary ducts, along with comedo necrosis. The surgical margins were free of carcinoma cells.

## DISCUSSION

DCIS represents a group of malignant lesions originating from a clonal proliferation of malignant epithelial cells of

the mammary ducts, without evidence of invasion beyond the basement membrane. DCIS is considered precancerous and, if left untreated, has a 30% to 50% risk of transformation into invasive carcinomas within 10 years.<sup>8</sup> Although complete surgical removal of the tumor is recommended for treatment of DCIS, evaluating the extent of intraductal spread of DCIS is difficult because many DCIS are detected only on imaging, not on palpation.<sup>9-11</sup> Although pioneers in the treatment of DCIS have adopted the mammography-guided hook-wire technique for the complete surgical removal of the tumor,<sup>12</sup> this technique is not image-guided in real-time and the accuracy of this technique cannot be guaranteed.<sup>13</sup>

There are several reported methods of image-guided preoperative marking for DCIS. Ultrasonographic examination is both convenient and real-time; however, the margin of the lesion can be unclear and in comparison with MRI findings and pathological results, the lesion size as determined by ultrasonography can be underestimated. In addition, real-time 3D ultrasound navigation<sup>14</sup> can only be used in a limited number of institutions. A method employing 3D helical CT and multidetector-row CT is considered easier to perform and requires no additional special equipment.<sup>15</sup> However, when compared with MRI of the same population, multidetector-row CT was less sensitive for detection of DCIS and detection of the presence of the intraductal component.<sup>16</sup> There is also the critical problem of radiation exposure when using CT. There have been many reports indicating that, when compared with mammography, MRI is useful for detecting the full extent of DCIS.<sup>17-19</sup> Therefore, MRI appears to be the best diagnostic modality for evaluating the extent of a nonpalpable DCIS and for determining intraductal spread in the planning of BCS. To improve surgical treatment for DCIS, there is a need to link the precise extent of DCIS detected by MRI directly to the surgical lesion.

Although the use of a prone MRI-guided hook-wire technique has been reported,<sup>20</sup> approaching the breast lesion during surgery is difficult. The localization of the lesion on breast MRI acquired in the prone position differs from that in the surgical position because of deformation of the breast under the effect of gravity. Tozaki and colleagues<sup>21</sup> reported on the use of MRI in the supine position, which is nearly the same position as the surgical position, when using the parallel acquisition technique for planning BCS. Sakakibara and colleagues<sup>6</sup> reported on a BCS approach that uses projection and reproduction techniques of breast MRI obtained in the surgical position. However, these techniques were not performed in real-time, and required precise repositioning of the patient while performing the subsequent surgery. Yamashiro and

colleagues<sup>22</sup> reported on an MRI marking technique for planning of BCS with patients in the supine position; however, they used MRI only for the modification of the first resection line, as determined by ultrasonography.

Compared with the techniques described previously, our novel preoperative MRI-guided marking technique functions in real-time and maintains the same patient position that is used during subsequent operation. The technique was made possible by using a recently developed real-time virtual reality navigation system with an open MRI scanner. Because the patient position is exactly the same as during subsequent operation, it is intuitive for surgeons to perform the dye marking procedure. The 3D navigation system facilitates an intuitive 3D representation of the needle and the target and depicts the needle and the tumor by creating polygon models in 3D space. It is possible to observe the arbitrary cross-sectional images and the 3D models of the volume of interest; a surgeon can intuitively access the target by referring to the 3D images. To use and operate the system and perform the surgery described in this study, surgeons are required to be experienced and proficient at performing breast surgery and to obtain training in the acquisition of orientation in a 3D virtual environment.

Because there is no extension of the breast, the precise marking of a resection line can be performed, which precludes overestimation of the lesion size. The system described here allows an accurate surgical approach to breast tumors that cannot be adequately visualized by other imaging modalities. Although diagnostic radiology with surgical position has not yet been established, all patients also underwent MR imaging with a high magnetic field closed-bore MRI. The images acquired with the open MR were compared with the images acquired with the conventional diagnostic closed-bore MR image.

The primary cause of the observed FRE is the image-to-patient registration. Deformation of soft tissues, such as skin, as well as respiratory motion, can affect the accuracy of registration. However, we consider the FRE determined in this series of procedures to be acceptable and sufficient for resection of the tumor, because the dye marking itself cannot be more precise. This suggests that currently, the reproducibility of the real-time virtual reality technique is adequate for guiding BCS. Although the current level of accuracy is acceptable for this type of operation, a nonrigid registration method that can account for soft tissue shifts and deformations might be required in the future to improve the accuracy of the surgical navigation system. The technique used in this study might also be applicable to other therapeutic modalities for different diseases, such as brain tumors or liver cancers. Promising results for treatment of the liver have been obtained.<sup>4</sup> Additional efforts

are needed to reduce errors in navigation and to widen its appreciation in the future.

Because of the long acquisition time of MR images, it took longer than usual to perform the navigation procedure. Imaging of the patient in the surgical position has the disadvantage of underestimating small intraductal spread because there is no extension of the breast in the surgical position. In addition, open MRI has a low magnetic field that can reduce the possibility of detecting lesions. To the best of our knowledge, this is the first report of BCS for DCIS using this class of technique. Our surgical approach might be clinically feasible for the surgical planning and management of patients with DCIS. Although advances continue to be made in the image-based diagnosis of breast cancer, surgical techniques will be improved if such navigation systems become widely established.

In conclusion, the real-time virtual reality navigation system using open MRI that we have developed is feasible for safe and accurate excision of breast tumors that were difficult to detect with palpation and ultrasonography. The navigation system was rated as very useful by 2 surgeons with experience in breast surgery. Users of the system require only experience in performing breast surgery and background training on how to acquire an orientation within a 3D virtual environment. Although long-term outcomes obtained when using the system will require further evaluation, this technique might offer improved outcomes without increasing the risk of major recurrence, and might promise a better quality of life for DCIS patients.

### Author Contributions

Study conception and design: Tomikawa, Hong, Shiotani  
Acquisition of data: Tomikawa, Hong, Shiotani, Tokunaga, Konishi, Ieiri, Tanoue, Akahoshi  
Analysis and interpretation of data: Tomikawa, Hong, Shiotani  
Drafting of manuscript: Tomikawa  
Critical revision: Maehara, Hashizume

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