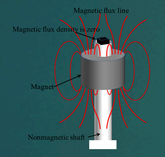
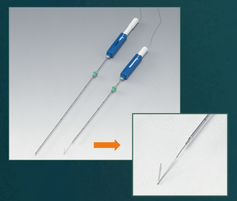
Introduction:

Non-palpable breast lesions represent about 25-35% of all breast cancers diagnosed in developed countries, according to findings based on the evolution of imaging modalities such as MRI, and the uses reliable biopsy techniques such as ultrasound-guided and stereo-guided vacuum assisted biopsies. Wire -guided localization (WGL), radio-guided localization (RGL), and SAVI SCOUT localization (SSL) have been presented as a surgical procedure for non-palpable breast lesions. The reported disadvantages of WGL are related to mechanical stimulation of wire plucking, kinking, and patient discomfort. RGL has issues regarding radioactive licensing, handling, and waste management, and the SSL system requires high start-up costs.
To eliminate these problems, we verified the magnetically guided localization (MGL) method for breast lesion localization by means of the combinations of the magnetic probe TAKUMI (Matrix cell Research Institute Inc., Tokyo, Japan) and the guiding-marker system®(Hakko, Tokyo, JAPAN). The TAKUMI is a novel handheld magnetic probe with a permanent magnet and a Hall magnetic sensor for detecting magnetic substances (**Fig. 1**). It was newly developed at the University of Tokyo under a grant from the Japan Agency for Medical Research and Development (AMED). TAKUMI is commercially available, has the regulatory approval in Europe for medical device safety (CE mark).



The magnetic field lines of the ring-shaped permanent magnet enclosed in the head of the magnetic probe. The magnetic sensor is located at the magnetic null point at the top of the magnet. Tiny variations in the magnetic fields can be detected without the offset attributes from the nonzero magnetic fields. The amplifier gain can be enhanced optimally for tiny magnetic signals.

Fig. 1 Magnetic probe TAKUMI® (Matrix cell Research Institute Inc., Tokyo, Japan)



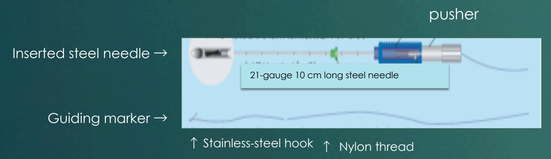
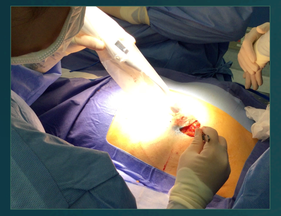


Fig. 2 Guiding-marker system® (Hakko, Tokyo, Japan)



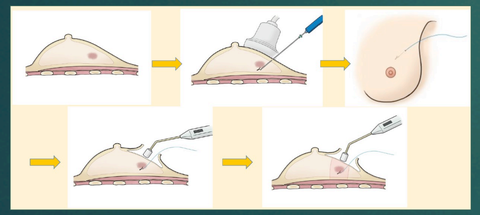


Fig. 3 All procedures of this clinical trial

References:

1. James R. Harvey, et al., Safety and feasibility of breast lesion localization using magnetic seeds (Magseed): a multi-centre, open-label cohort study. Breast cancer Research and Treatment, 2018. 169: 531-536
2. Priya H. Jadeja, et al., Utilization of multiple SAVI SCOUT surgical guidance system reflectors in the same breast: A single institution feasibility study. The Breast Journal , 2017. Vol.24
3. M. Ahmed, et al., Magnetic sentinel node and occult lesion localization in breast cancer (MagSNOLL Trial). Wiley Online Library, 2015 online, DOI:10.1002/bjs.9800
4. Adam D. Gerrard, et al., Surgeoun-led intraoperative ultrasound localization for nonpalpable breast caners: results of 5 years of practice. Clinical Breast Cancer 2019

Patients and Methods:

Patients were enrolled in this multi-center, open-label trial from January 2019 to March 2019 at two University Hospitals. The inclusion criteria were age 20 or older female patients who had non-palpable breast lesions, for which breast-conserving surgery or tumor resection was performed (**Table 1**). Patients who were pregnant or had metal allergy or inflammatory breast cancer were excluded. The guiding-marker system® consists of a stainless-steel hook (φ 0.28 x 10 mm) connected with a nylon thread and a 21-gauge 10 cm long steel needle (**Fig. 2**). The marker was inserted into the center of the target lesions using ultrasound guidance or stereo guidance within 4 days before surgery. The TAKUMI was used to determine whether the guiding marker was detectable or not, before, during, and after the surgical resection of the specimen(Fig. 3). The removal rates of the guiding marker, surgical margin status, and re-operation rates were evaluated as the primary outcomes, and the volume and weight of the excised specimen were evaluated as secondary outcomes. The aim of this study was thus to evaluate the feasibility and safety of MGL. The study protocol of the evaluation of magnetic probe system for detecting non-palpable lesions of the breast was approved by the Institutional Review Board of Nippon Medical School Foundation (CRB3180001) and was registered at https://jrct.niph.go.jp/re(protocol record jRCTs032180422). Written informed consent was obtained from all participants.

	n= 41
Age	54.4yrs.
BMI, median (range)	21.8 (17.9-30.4)
Diagnosis Benign, n (%) Indeterminate/ suspicious for malignancy, n (%) Malignancy, n (%)	 2 (4.9%) 3 (7.3%) 36 (87.8%)
Operation Tumorectomy ; Tm, n (%) Partial mastectomy ; Bp, n (%)	 5 (12.2%) 36(87.8%)
Neoadjuvant chemotherapy (NAC), n (%)	7 (17.1%)
Premenopausal, n (%) Postmenopausal, n (%)	15 (36.6%) 26 (63.4%)
Tumor status Micro-calcification, n (%) Tumor lesion, n (%) Tumor size, median (range)	 5 (12.2%) 36 (87.8%) 1cm (0.5-2.3cm)

Table 1. Patient and tumor characteristics

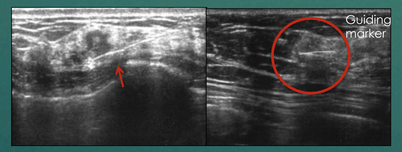


Fig. 4 Ultrasound image during and after insertion of marker

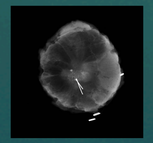
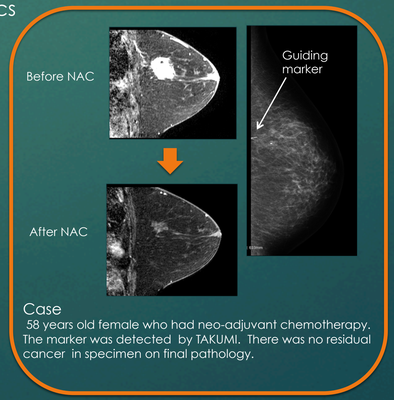


Fig. 5 X-ray image of specimen with micro-calcifications



Case
58 years old female who had neo-adjuvant chemotherapy. The marker was detected by TAKUMI. There was no residual cancer in specimen on final pathology.

Diagnosis on final pathology (n=41) Benign, n (%) DCIS, n (%) Invasive carcinoma, n (%) Pathological complete response after NAC, n (%)	 2 (4.9%) 7 (17.1%) 26 (63.4%) 6 (14.6%)
Specimen Status Specimen weight, g (range) Specimen volume, ㎤ (range)	 34.5g (2-131g) 39.01㎤ (0.012-240㎤)
Intraoperative frozen section analysis (Total=39) Positive, n (%) Intraoperative re-excision rate, n (%)	7 (17.9%) 3 (7.6%) 2 (5.1%)
Margin Status on final pathology Positive, n (%) Negative, n (%) 5mm <, n (%) 5mm ≥, n (%)	Total=39 1 (2.6%) 38 (97.4%) 30 (76.9%) 8(20.5%)
Re-excision rate on subsequent surgery n (%)	Total=39 1 (2.6%)
Boost radiation rate n (%)	Total=39 8 (20.5%)

39 cases

Table 2. The results of final pathology and the clinical outcome

Results:

Forty-one patients were recruited into this study. Thirty-six patients (87.8%) underwent breast-conserving surgery for breast cancer treatment, and 5 (12.2%) underwent tumor resection for biopsy purposes. All guiding markers were removed during the initial surgical operation. Three out of 39 breast cancer patients (7.6%) were diagnosed as margin positive in frozen section analysis; 2 (5.1%) underwent additional resection during the initial surgery, and 1 (2.4%) underwent subsequent surgery due to the positive margin on final pathology. Eight patients (19.5%) underwent boost radiation therapy due to the close margin. The median weight of all excised specimens was 28 g. The range was wide (2-131 g) and depended on the expanse of the lesion. No complications or adverse events were recorded in relation to either the marker placement or the surgery (**Table 2**). All guiding markers were detectable before, during, and after the surgical resection of the targeted lesions with TAKUMI.

Discussion:

Multiple techniques have been described to minimize the incidence of positive or close margins, such as RGL, WGL, SSL, intraoperative US by surgeons, use of preoperative MRI and large-volume lumpectomy. The wider margin is preferable for margin clearance, but it tends to lead poor cosmetic outcome of the conserved breast. On the other hand, the narrower margin tends to be diagnosed as positive surgical margins.
In this study, this MGL technique could detect the guiding marker and gave us pinpoint orientation of the target lesions before, during, and after the surgery. As a result, MGL can make it possible to remove smaller volume of breast tissue with the targeted lesion. It provides satisfactory cosmetic outcomes, and it may also decrease medical costs by decreasing reoperation rate. Surgeons could perform these procedure without anxiety.

Conclusion:

This feasibility study demonstrated that the combination of the guiding system and the magnetometer, TAKUMI, could be used for localization of non-palpable breast lesion. These data clearly show that MGL is a reliable, accurate, and convenient localization system for non-palpable breast lesions. This technique has no disadvantages of WGL, RGL, and SSL.

Conflicts of Interest:

The authors declare that they have no conflicts of interest.