Assessing the value of volume navigation during ultrasound-guided radiofrequency- and microwave-abelations of liver lesions

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\textbf{A B S T R A C T}

\textbf{Purpose:} The goal of our study was to determine the influence of ultrasound (US)-coupled volume navigation on the use of computed tomography (CT) during minimally-invasive radiofrequency and microwave ablation procedures of liver lesions.

\textbf{Method:} Twenty-five patients with 40 liver lesions of different histological origin were retrospectively analysed. Lesions were ablated following standard protocol, using 1) conventional US-guidance, 2) manual registered volume navigation (mVNav), 3) automatic registered (aVNav) or 4) CT-guidance. In case of ultrasonographically inconspicuous lesions, conventional US-guidance was abandoned and mVNav was used. If mVNav was also unsuccessful, the procedure was either continued with aVNav or CT-guidance. The number, size and location of the lesions targeted using the different approaches were documented.

\textbf{Results:} Of the 40 lesions, sixteen (40.0\%) could be targeted with conventional US-guidance only, sixteen (40.0\%) with mVNav, three (7.5\%) with aVNav and five (12.5\%) only through the use of CT-guidance. Of the three alternatives (mVNav, aVNav and CT only) the mean size of the lesions targeted using mVNav (9.1 \pm 4.6 mm) was significantly smaller from those targeted using US-guidance only (20.4 \pm 9.4 mm; \(p < 0.001\)). The location of the lesions did not influence the selection of the modality used to guide the ablation.

\textbf{Conclusions:} In our cohort, mVNav allowed the ablation procedure to become less dependent on the use of CT. mVNav supported the ablation of lesions smaller than those that could be ablated with US only and doubled the application of minimally-invasive US-guided ablations.

\begin{section}
\section{1. Introduction}

The success of radiofrequency (RFA) and microwave ablation (MWA) procedures is directly dependent on accurate lesion localization and applicator placement. To guide applicator placement, RFA and MWA procedures are generally performed under image guidance of ultrasound (US), computed tomography (CT) or magnetic resonance (MR) imaging \cite{1,2}. Of the three technologies US-guidance is most practical; The real-time image guidance provided by US enables beginning to end monitoring of the procedure and when required allows for adaptation of the electrode insertion path at lower costs compared to the other imaging modalities \cite{3,4,5,6,7}. However, lesions can be inconspicuous on US as a consequence of e.g. isoechogenicity, small size, subphrenic localization, (macronodular) cirrhosis, or patient habitus \cite{2,3,4,5,6,7,8,9,10,11}. In fact, Rhim et al. \cite{12} reported that the inability to visualize lesions on US accounted for 55.8\% of the lesions that could not be ablated using conventional US-guidance.

A possibility to overcome this shortcoming is the use of navigation in three-dimensional (3D) pre-interventional imaging data sets. Navigation approaches help overcome all kinds of shortcomings of interventional imaging modalities such as fluorescence imaging, gamma-ray guidance, and US \cite{13,14,15,16,17,18}. For the latter, volume based navigation (VNav) can be realized by manual and/or automatic co-registration of US-images with (pre-)interventional acquired CT- or MR-imaging data sets \cite{19,20,21,22}.

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Although the technology is being implemented, few studies have reported on the technical feasibility of this approach [8,15,23]. This particular study focused on establishing how manual registered volume navigation (mVNav) could help reduce the usage of interventional CT during US-guided ablations of liver lesions.

2. Material and methods

2.1. Patients

All patients scheduled for an ablation procedure of liver lesions between August 2015 and February 2016 were retrospectively included in the study after obtaining written informed consent. This study was conducted in accordance to the 1964 Helsinki Declaration and its later amendments, and received a certificate of no objection by the Medical Ethical Committee of our institute.

25 patients with, in total, 40 lesions were included: 23 hepatocellular carcinomas (HCC), 11 colorectal metastases, four bronchocarcinoid metastases and two (choroidal) melanoma metastases. Demographic, liver and lesion specific information is presented in Table 1. Liver cirrhosis and the aetiology of the cirrhosis were evaluated next to the type, size (largest diameter measured on the most recent CT- or MR-imaging) and location of the lesion.

2.2. Pre- and post-interventional imaging

Diagnosis of the lesion type was based on imaging (n = 22 patients) or biopsy histology (n = 3 patients). The CT- and MR-images that provided the basis for navigation were derived from diagnostic multiphase contrast-enhanced CT (CE-CT) or dynamic gadolinium-enhanced MRI scans [24].

A contrast-enhanced CT-scan (CE-CT) was performed on an Aquilion 16 (Toshiba Medical Systems, Otawara, Japan) after the ablation procedure (in the same session; Fig. 1). Technical success was defined as described by Ahmed et al. [25].

2.3. Navigation hardware

The Logiq E9 with XDclear (General Electric (GE) Healthcare, Little Chalfont, Buckinghamshire, United Kingdom) US system was used and combined with a driveBAY™ (Ascension Technology Corp., an NDI company, Shelburne, Vermont, USA) and the HS Amica™ (HealthTronics, Austin, TX, USA) were used for RFA and MWA procedures, respectively. The ablation system used depended on the operator’s preference and e.g. nearby located structures that could induce the heat sink effect.

Table 1

| Characteristics                     | Patients (n = 25 (100 %)) | Mean size ± SD (mm) |
|-------------------------------------|---------------------------|---------------------|
| Patients with liver cirrhosis (n = 13 (52.0 %)) | - Male: 17 (68.0 %)        | 16.8 ± 7.9          |
| - Female: 8 (32.0 %)                 |                           | 17.9 ± 3.4          |
| Lesions (n = 40 (100 %))            |                           | 13.7 ± 9.6          |
| Median of lesions per patient (range)| 1 (1–4)                   |                     |
| HCC                                 | 23 (57.5 %)                |                     |
| Mean size ± SD (mm)                 | o 17 (42.5 %)              |                     |
| - Metastases                         | o 13.7 ± 9.6              |                     |
| n = amount; SD = standard deviation; HCC = hepatocellular carcinoma; mm = millimeter. | | |
2.6. VNav error measurements

During navigation a lesion could become visible on US to the interventionalist after VNav indicated its location. In this case the error of the registration could be measured by determining the distance between the target point set in the CT- or MR-images and the center of the lesion visible on US.

2.7. Statistical analyses

For the statistical analyses SPSS version 23 (IBM SPSS Statistics, IBM Nederland BV, Amsterdam, the Netherlands) was used. The independent-samples t-test and ANOVA were used for comparison of mean values, the Fischer’s exact test for comparing nominal variables. For comparison of the lesions between the guidance modalities αVNav and CT-guidance were combined; This group consisted of lesions that were not possible to ablate with either US-guidance or mVNav. A p-value

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![Fig. 1. US-based navigation setup.](image1)

**Fig. 1.** US-based navigation setup. (a) The setup of the CT intervention suite with US system and electro magnet. The setup for manual registered VNav is shown in (b) and automatic registered VNav in (c) with the active tracker placed on the patient. The magnet has to be placed near the workfield to track the sensors attached to the transducer and active tracker (arrow)(d).

![Fig. 2. Flowchart demonstrating the distribution of the lesions over the guidance modalities used for ablation.](image2)

**Fig. 2.** Flowchart demonstrating the distribution of the lesions over the guidance modalities used for ablation. The lesion shown with the dashed arrow was targeted under CT-guidance, because conventional US identification was complicated after a pneumothorax occurred during the first puncture.
<0.05 was considered statistically significant.

3. Results

3.1. Application of interventional guidance approaches

Seventeen of 25 patients (68.0%; n = 26 lesions) were treated with

Fig. 3. Clinical examples of the value of VNav. Using mVNav the lesion could not be seen with conventional US imaging (a), even though they are compared with diagnostic MR images (b). However, a target was set on the lesion using the MR image and the target icon (T) appears on the US image as well. Now, VNav gives an indication of its location. An electrode was inserted (white arrows) towards the target under guidance of the mVNav (c and d). The pre-interventional MR images (e) are compared to the post-interventional CT-images (f). The lesion (red arrow) appears to be inside the ablation zone (blue arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).
RFA (15 with 3 cm and two with 4 cm exposure electrodes). Eight of 25 patients (32.0 %; n = 14 lesions) were treated with MWA.

Thirty-two of the 40 ablated lesions were ablated using a single applicator and eight using multiple applicators. Sixteen of 40 lesions (40.0 %) were targeted using conventional US-guidance, sixteen (40.0 %) were targeted using mVNav, three (7.5 %) using aVNav, and five (12.5 %) with CT-guidance (Fig. 2). One lesion that could be identified with conventional US was ablated under CT-guidance; a pneumothorax after the first puncture complicated further US identification (Fig. 2).

Image data sets used for mVNav were derived from CT or MR (both in eight lesions). Post-ablation CE-CT showed an overall technical success rate of 95 % (38 of 40 lesions). This was 93.8 % (15/16) for conventional US-guidance, 100 % (16/16) for mVNav, 100 % (3/3) aVNav and 80 % (4/5) for CT-guidance.

23 of 40 lesions (57.5%; Fig. 2) were initially not visible on conventional US (n = 16; 40.0 %) or the interventionalist was uncertain about the location (n = 7; 17.5 %). The interventionalist was able to target 69.6 % (16 of 23) of these lesions with mVNav. This resulted in a two-fold increase in the number of lesions that could be targeted efficiently using US-guidance (80.0 % in total; Fig. 2).

To adjust the mVNav registration after plane-lock, the interventionists used a median of three landmarks (range 1–4). In 56.3 % of the ablations performed using mVNav (9 of 16), the interventionalist placed the applicator(s) in the lesion only based on the virtual feedback provided by the navigation set-up (Fig. 3).

3.2. Lesion characteristics versus guidance modality

The mean size (± SD) of the lesions was 15.5 ± 8.7 mm (range 5.0–36.0 mm). Lesions targeted by mVNav (9.1 ± 4.6 mm) were significantly smaller than lesions targeted using conventional US-guidance (20.4 ± 9.4 mm, p < 0.001)(Fig. 4). The mean size of the lesions targeted by aVNav (16.7 ± 9.1 mm) or CT-guidance (19.5 ± 3.8 mm) did not differ from those targeted using conventional US-guidance (p = 0.542 and p = 0.845, respectively). In patients where mVNav was applied and the error could be measured, the mean navigation inaccuracy was 5.7 ± 2.3 mm (mean ± SD; range 3.00–9.00 mm; one missing value; seven lesions).

Comparison between the three guidance groups (conventional US-guidance, mVNav, or aVNav and CT-guidance) did, however, not reveal a clear difference in: 1) the distribution of lesion types (p = 0.060), 2) the presence of liver cirrhosis (p = 0.801), or 3) the anatomical location wherein the lesions occurred (measured over preference for segment 8 (p = 0.360), left or right lobe (p = 0.409), or the individual segments (p = 0.221)).

3.3. Follow up

Long-term follow-up revealed a recurrence rate of 52 % on patient basis at 29–33 months. Recurrence-free survival is shown in Fig. 5.

4. Discussion

This study emphasizes the value of mVNav on US-guided RF and MW ablations, for the complementary use of mVNav doubles the number (from 40 to 80 %) of US-guided ablations. In 69.6 % (16 of 23) of the lesions that could not be targeted using conventional US-guidance, the lesions could be targeted with mVNav, which is in line with the expectations expressed by Lee et al. [15]. Hence, mVNav may be considered a minimal invasive alternative for CT-guidance, resulting in less radiation exposure for the patient and interventionalist, lack of need for contrast medium, lower costs and improved logistics.

A small lesion size appeared the most frequent limitation of conventional US-guidance ablations and is in line with limitations found in other studies [3,12], however, mVNav supported the ablation of significantly smaller lesions. The mean size of the lesions ablated under aVNav or CT-guidance did not differ from the size of lesions ablated under conventional US-guidance, but were not able to be ablated with mVNav guidance. It is uncertain why this is the case, since there was no difference in the location of the lesions or presence of liver cirrhosis.

The amount of lesions that were not visible using conventional US-guidance (n = 16; 40.0 % in the total group) is in line with the 27 % invisibility rate reported by Kim et al. [2]. When the uncertainty of the interventionalist was also taken into account, the invisibility rate in this
study increased with 17.5 % (total of 57.5 %). Uncertainties are e.g. mistaking cirrhotic nodules for lesions (pseudolesions), or poor conspicuity of the lesion [26]. This is in line with 16.7 % of pseudolesions and 7.4 % of mistargeting reported earlier by Lee et al. [15].

The recurrence rate of 52 % found in this study also corresponds to the recurrence rate of 43.4 % and 59.8 % for 2 and 3 years follow-up reported by Tateishi et al. [27].

The registration method used for mVNav was based on plane-registration [28,29,23]. Plane registration can be considered a less accurate manual registration procedure compared to point-registration, however it was considered to be more practical [23], because identification of well-defined landmarks for point registration can be difficult in patients [30]. Use of an additional registration point allowed for refinement of the planar registration [30,23].

We found a registration error of 5.7 mm with mVNav which is in line with the 5.8 mm found by Krücker et al. (2007) [31].

The use of an active tracker in the aVNav set-up limited the chance of manual (human) error and reduced position artefacts encountered between the acquisition of the CT-scan used for navigation and the interventional setting. An obvious question that arises is: Which of the two navigation procedures, mVNav or aVNav, did we consider most valuable? The sequential order (US-guidance, mVNav, aVNav, CT-guidance) of the current study did not allow for a definite head-to-head comparison. However, the order itself already provides valuable information as mVNav is more easily applied as it does not require interventional CE-CT.

Although an explicit influence of the navigation was seen on the number of lesions that could be treated without CT, the current study was limited by its retrospective design and the limited number of patients included. To fully strengthen the current findings, a prospective study that evaluates VNav in ultrasonographically inconspicuous liver lesions in a large (randomized) group of patients is recommended. Furthermore, next to the impact navigation has on the number of lesions that can be successfully treated without CT guidance, it would also be very interesting to investigate the influence that such navigation has on the dexterity and decision-making of the interventional radiologist during the US-guided procedure. In different medical fields (e.g., surgery), such concepts are increasingly used to study the influence a technology has on the procedural performance of the specialist [32].

5. Conclusion

Integrating an mVNav set-up in our study doubled the number of lesions that could be treated using minimally-invasive US-guided ablation. mVNav also supported the treatment of smaller lesions. Evaluation of this technology in a larger patient cohort is recommended to strengthen these results.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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CRediT authorship contribution statement

Philippa Meershoek: Investigation, Writing - original draft, Visualization. Nynke S. van den Berg: Formal analysis, Writing - review & editing. Jacob Lutjeboer: Investigation, Writing - review & editing. Mark C. Burgmans: Investigation, Writing - review & editing. Rutger W. van der Meer: Investigation, Writing - review & editing. Catharina S.P. van Rijswijk: Investigation, Writing - review & editing. Matthias N. van Oosterom: Formal analysis, Writing - review & editing. Arian R. van Erkel: Methodology, Supervision, Investigation, Writing - review & editing. Fijs W.B. van Leeuwen: Conceptualization,
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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi: https://doi.org/10.1016/j.ejro.2021.100367.

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