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IMAGING DI FUSIONE E NUOVE TECNOLOGIE ABLATIVE IN ONCOLOGIA INTERVENTISTICA

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RESEARCH PROJECT

Tumor ablation by means of other than traditional surgical approaches is a methodology attempted with modest success for a number of years. During the past few years however, the use of image-guided interventions in cancer treatment has experienced unparalleled growth. Modern approaches take advantage of the vastly superior armamentarium of imaging strategies now available. Advances in material science, and methods for delivery of ablating agents combined with improved localization now make possible to be much more aggressive and effective in attempting to achieve local ablation of malignant tumors. Interventional Oncology is gaining increasing acceptance as a viable alternate or complementary treatment for a variety of cancers.

Ongoing research in industry and academic centers is focused on two clinical needs: to overcome limitations of current imaging modalities in guiding and monitoring ablation procedures and to produce larger zones of ablation in different organs in a safe and reproducible fashion.

Ultrasound (US) is considered as imaging modality of choice for guiding percutaneous ablation procedures in the liver, with computed tomography (CT) guidance being reserved for lesions inconspicuous on US. However, there are occasions when the liver lesion is only optimally visualized on contrast-enhanced CT and magnetic resonance (MR) imaging, making targeting and monitoring difficult, due to lack of real-time imaging guidance. Given the advantages of US guidance, it would be ideal if the procedure can be performed with real-time US matched with supplementary information from contrast enhanced CT or MR images. Fusion imaging, the process of aligning and superimposing images obtained using two different imaging modalities, is a rapidly evolving field of interest, with its own specific operational conditions. The Phase I of this Research Project was designed to investigate the feasibility and validity of real-time guidance using a virtual navigation system that fused US and CT information in

targeting and ablating, by means of radiofrequency, a liver target inconspicuous on US.

Phases II and III were designed to assess feasibility and safety of new ablative technologies in lung ablation in experimental animal models. In Phase II multitined perfused electrode needles were used to perform radiofrequency ablation of rabbit lung tissue. The potential benefits of using saline-enhanced RF ablation could be important in lung ablation, because of the tissue characteristics of the lung. In fact, air containing lung tissue has a naturally high tissue impedance, and this makes difficult to create a safety margin around the treated lesion . On the other hand, direct and uncontrollable thermal damage to adjacent and remote structures was observed more frequently using saline infusion during RF ablation than conventional RF ablation. The aims of Phase II were therefore to assess feasibility and safety of RF ablation of lung tissue performed with multitined perfused electrodes.

Together with new RF devices, also alternative sources of energy are under investigation to overcome conventional RF ablation limits. With several theoretic and practical advantages, microwave (MW) ablation is a promising new option in the treatment of surgically unresectable tumors. The potential benefits of MW technology include consistently higher intratumoral temperatures, larger tumor ablation volumes, faster ablation times, improved convection profile and less procedural pain. Phase III was designed to know how MW ablation affects normal lung tissue, comparing a prototype MW ablation system with a commercially available RF device in an in-vivo lung rabbit model.

LIVER LESIONS TARGETING AND ABLATION WITH A FUSION IMAGING SYSTEM: AN EXPERIMENTAL FEASIBILITY STUDY

ABSTRACT

Purpose: To investigate the feasibility and validity of real-time guidance using a fusion imaging system that combined ultrasound (US) and computed tomography (CT) in the targeting and subsequent radiofrequency (RF) ablation of a liver target inconspicuous on US.

Methods and Materials: The study was designed as an experimental ex-vivo study in calf livers with radiopaque internal targets, inconspicuous at US, simulating a focal liver lesion. The study included two phases. The initial phase was to examine the feasibility of matching pre-procedural volumetric CT data of the calf livers with real-time US using a commercially available multimodality fusion imaging system (Virtual Navigator System, Esaote SpA, Genoa, Italy), and to assess the accuracy of targeting using a 22 gauge (G) cytological needle using the system. The second phase of the study was to validate such a technique using a 15G RF multitined expandable needle (RITA Medical Systems, Mountain View, CA) and to examine the accuracy of the needle placement relative to the target. Unenhanced CT of the liver and multiplanar reconstructions were performed to calculate respectively the distance between the needle and the pellet and the distance between the central tine of the RF electrode and the pellet.

Results: All calf livers underwent successful CT-US registration with a mean registration error of 0.30 ± 0.01 cm and 0.29 ± 0.01 cm in the initial and second phase of the study, respectively. In the initial phase an overall number of 24 insertions were performed following the US-CT guidance. The needle to target distance was 1.9 ± 0.7 mm (range 0.84-3 mm). In the second phase an overall number of 12 ablations were performed and only one insertion was done to place the electrode following the US-CT guidance. The mean target-central tine

distance, recorded at post-procedural CT, was 3.9 ± 0.7 mm (range 2.94-5.14 mm).After the dissection of the specimen the pellet was found unchanged in the center of the ablation zone in all cases

Conclusion: Real-time registration and fusion of pre-procedure CT volume images with intra-procedure US is feasible and accurate. For lesion hardly visible at US or CT or for more complex procedures, such as thermal tumor ablations that require positioning of multiple applicators and puncture of multiple lesions, navigation systems might be of help to reduce puncture risk and procedure time and to allow for more complete and radical therapy.

INTRODUCTION

Image guidance is essential in the treatment of liver tumors using percutaneous ablative techniques. Apart from careful pre-procedure planning and elaborate post-procedure evaluation, accurate intra-procedure targeting, monitoring, and controlling play a critical role in the success of the technique [1].

In our centre radiofrequency (RF) ablation is most commonly performed under ultrasound (US) guidance, with computed tomography (CT) guidance being reserved for lesions inconspicuous on US. However, there are occasions when the liver lesion is only optimally visualized on contrast-enhanced CT and magnetic resonance (MR) imaging, making targeting and monitoring difficult due to lack of real-time imaging guidance. In this scenario, it would be desirable to fuse information from different imaging modalities (e.g., US and CT) and such multimodality matching have been utilized in nuclear medicine, radiotherapy, and neurosurgery [2-4] .

In this study, we investigate the feasibility and validity of real-time guidance using a fusion imaging system that combined US and CT information in the targeting and subsequent RF ablation of a liver target inconspicuous on US.

MATERIALS AND METHODS

Study Design

The study was designed as an experimental ex-vivo study in calf livers with radiopaque internal targets simulating a focal liver lesion. The approval by local Research Ethics Committee was obtained. The study included two phases. The initial phase was to examine the feasibility of matching pre-procedural volumetric CT data of the calf livers with real-time US using a commercially available multimodality fusion imaging system (Virtual Navigator System, Esaote SpA, Genoa, Italy), and to assess the accuracy of targeting using a 22 gauge (G) cytological needle using the system. The second phase of the study was to validate such a technique using a 15G RF multitined expandable needle and to examine the accuracy of the needle placement relative to the target.

Target

Radiopaque targets were represented by 1.5mm lead pellets, inconspicuous on conventional US but with high attenuation on CT. They allow realistic puncture by either of the needle types employed in our study. The pellet was implanted into calf liver, by using an 11 G soft introducer, 13 cm in length (StarBurst Soft Tissue Access System, RITA Medical System, Mountain View, CA). Soft introducers can be used with multitined expandable electrode needles, for the coagulation and ablation of soft tissue. They have a flexible sheath with a tapered tip and a blunt edge and a stainless steel stylet with three-face trocar point for cutting and dilation of tissue. In this study we used these introducers to place the bullets inside the calf liver. The introducer was inserted into the liver parenchyma from lateral liver side, to avoid the disruption of superior liver surface. After removing the stainless steel stylet, the pellet was put into the sheath and pushed inside the liver by means of the stylet. In each calf liver 4 pellets were inserted.

Fusion Imaging System

The system consists of an US scanner connected to the Navigation unit. The two units are connected by a video cable to grab the ultrasound screen and a network cable to query the current scan geometry of the US scanner. An electromagnetic tracking system, composed by a transmitter and a small receiver (mounted on the US probe) provides the position and orientation of the US probe in relation to the transmitter. This permits a correct representation in size and orientation of the second modality image. These data are provided by the US scanner by the network connection and automatically updated at every change on the console of the Navigation unit. The system specifications are provided in Tab.1.

The electromagnetic tracker is sensitive to metallic objects close or near the receiver or transmitter. Thus, any metallic material that may interfere and disturb the magnetic field must be avoided between the transmitter and the receiver.

Fusion Imaging System Setup

Prior to the intervention a four-step protocol was followed:

1. Ten 1.5mm radio-opaque fiducial markers (X-Spots, Beekley, Bristol, CT) were applied to the calf liver capsule, in order to correlate (register) the CT scan with the US scan.
2. Pre-procedure unenhanced multidetector CT (MDCT) of the liver was then performed using a 4-row scanner (LightSpeed Plus CT ,GE Medical Systems, Milwaukee, Wis) with a 1.25 mm collimation and a reconstruction interval of 0.6 mm, covering the external markers.
3. The CT DICOM series were transferred to the Virtual Navigator System by using the Picture Archiving and Communicating System (PACS).
4. The navigation system is coupled with an US machine (Technos MPX; Esaote, Genoa, Italy) and registration of the position of each fiducial marker to the system was executed in 2 stages. First the positions of all the

fiducial markers in the CT volume were identified and numbered (Figure 1a). Secondly the corresponding positions on the cow livers were matched by applying point contact with a registration pin (Figure 1b) from the system on each marker. The sequence was in accordance with the number given during the first stage. Accuracy or error of registration will be displayed by the system following completion of registration of all the 10 positions (Figure 1c).

Real-time US of the calf livers was then performed using a 3.5Hz curvilinear probe with the images being displayed on the monitor of the Virtual Navigator System, next to the corresponding CT volumetric images. A sterilizable biopsy kit for convex array (ABS 421, Esaote, Genoa, Italy), with a biopsy needle angle of 20° was used to guide the needle insertion. The US images could also be reverted to CT images on the same screen. Accuracy of the matched US-CT images was also subjectively assessed by the operator, using specific anatomical markers (i.e. air within liver vessels)

Phase I: Targeting

This was performed in 3 calf livers. The target was identified on the 'real-time' CT images during US assessment. As it was inconspicuous on US, the target was marked on the CT image and the corresponding location was pointed out by the system on the US image. The optimal biopsy route was chosen and a biopsy track was visualized (Fig. 2).

A 21 G cytological needle 20 cm in length (Quinjekt, Hospital Service, Roma, Italy) was advanced into the liver parenchyma under real-time ultrasound visualization, with the attached biopsy kit (Fig. 3). The tip of the needle should ideally be placed in the target, but given the small dimensions and the solid nature of it, we considered to go the nearest as possible to the pellet. Two targeting procedures were performed per pellet, by two radiologists experienced in CT- and

US-guided percutaneous interventions. Only one needle pass had to be performed for each targeting procedure. The accuracy of targeting was assessed on a repeat CT examination with the needles in-situ. Unenhanced MDCT of the liver was performed with a 1.25 mm collimation and a reconstruction interval of 0.6 mm, covering the entire liver. The distance between the needle and the pellet was calculated on multiplanar reconstructed CT images (reconstruction interval of 1 mm), along a plane perpendicular to the needle.

Phase II: Radiofrequency ablation of the target

RF ablation was performed in 3 calf livers. Target localization was performed and a 15 G RF multitined expandable electrode needle (Starburst XL, RITA Medical Systems, Mountain View, CA) was inserted into the liver using real-time guidance and biopsy kit, considering the target as the ideal centre of the ablation. The tip of the trocar was placed 1 cm from the centre of the intended ablation area (i.e. the pellet) for a 3 cm ablation, according to the manufacturer recommendations (Fig. 4). Following deployment of the tines to 3 cm, RF ablation was performed with a 200-W generator (model 1500; RITA Medical System, Mountain View, CA) at target temperature of 95 °C for 15 minutes. Continuous real-time US monitoring was performed during RF ablation. The target is heat resistant and therefore remained intact allowing visualization on a repeat CT post procedure. Only one needle pass had to be performed for each ablation procedure. Following ablation, the accuracy of targeting was assessed on a repeat CT examination with the needles in-situ. Unenhanced MDCT of the liver was performed with a 1.25 mm collimation and a reconstruction interval of 0.6 mm, covering the entire liver. The distance between the central tine and the pellet was calculated on multiplanar reconstructed CT images (reconstruction interval of 1 mm), along a plane perpendicular to the electrode. The liver was then cut along the electrode axis and the accuracy of RF targeting was assessed.

Results analysis

Registration error due to matching misalignment is expressed in cm by the navigation system. Results are expressed as mean ± SD for continuous data. Target accuracy is defined as the distances in mm between the epicentre of the target and the Chiba needle in the first phase of the study, and the distances in mm between the epicentres of the target and the tip of the central tine of the multitined RF electrode needle in the second phase.

RESULTS

All calf livers underwent successful CT-US registration with a mean registration error of 0.30 ± 0.01 cm and 0.29 ± 0.01 cm in the initial and second phase of the study, respectively.

After some experience in setting up the navigation system we were able to perform the system setup including the registration within 3-5 min.

In phase I each pellet was used for two US-CT guided targeting insertions. An overall number of 24 insertions were performed with the aim of placing the Chiba needle the nearest as possible to the pellet, following the US-CT guidance. The needle to target distance was 1.9 ± 0.7 mm (range 0.84-3 mm) (Fig. 5).

In phase II each pellet was used for one US-CT guided ablation. An overall number of 12 ablations were performed and only one insertion was done to place the electrode 1 cm from pellet, following the US-CT guidance. The mean target-central tine distance, recorded at post-procedural CT, was 3.9 ± 0.7 mm (range 2.94-5.14 mm).

After the dissection of the specimen the pellet was found unchanged in the center of the ablation zone in all cases (Fig.6).

Table 1. System specifications

Module	Description
US Scanner	Technos ^{MPX} Esaote S.p.A
US Probe	Convex array 6-2 MHz
Network connection	TCP/IP protocol
Navigation Unit	Virtual Navigator Esaote S.pA
Tracking system	PCIBirds (ASCENSION TECNOLOGY) Degrees of freedom: Six (position and orientation) Translation range, any direction: Standard transmitter = +/- 30 (76.2 cm) Angular range: All attitude Static accuracy standard sensor: .040 (1.0 mm) RMS position 0.15 degree RMS orientation

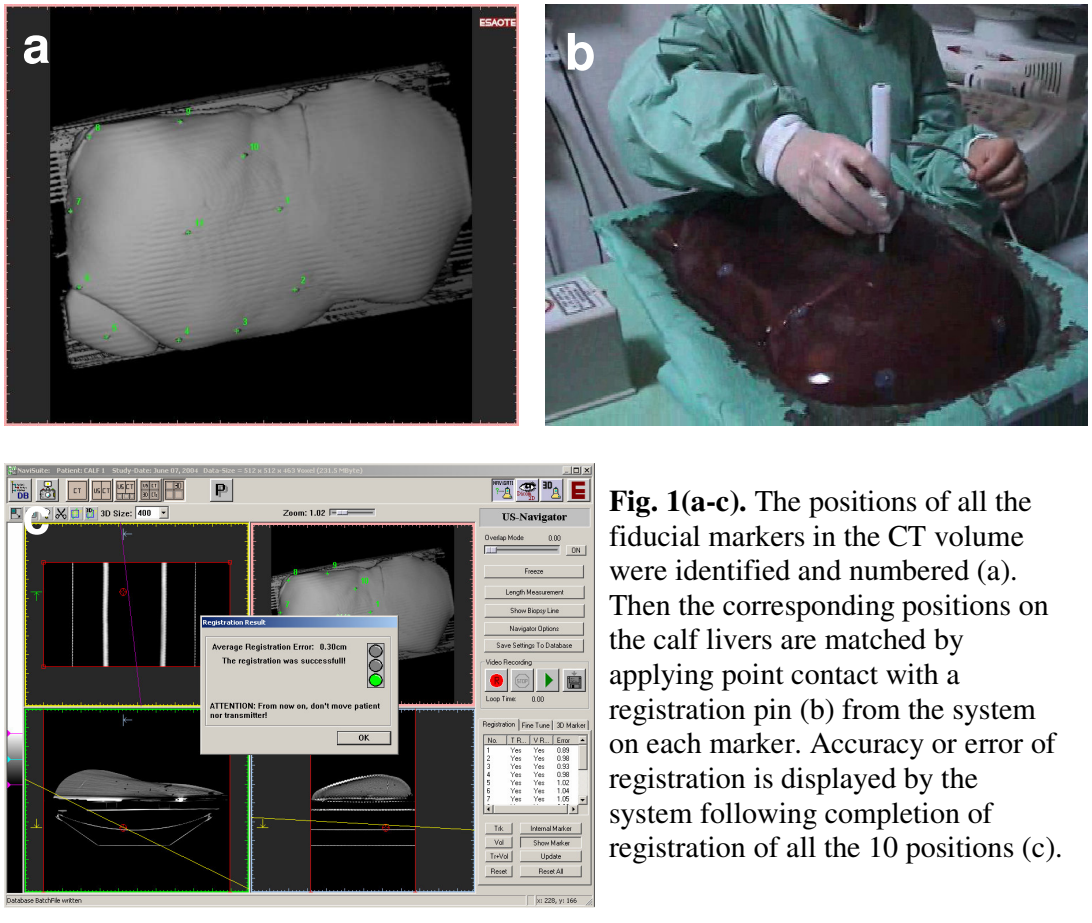

Fig. 1(a-c). The positions of all the fiducial markers in the CT volume were identified and numbered (a). Then the corresponding positions on the calf livers are matched by applying point contact with a registration pin (b) from the system on each marker. Accuracy or error of registration is displayed by the system following completion of registration of all the 10 positions (c).

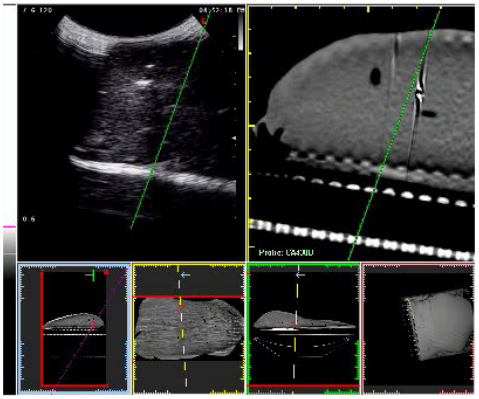

Fig.2

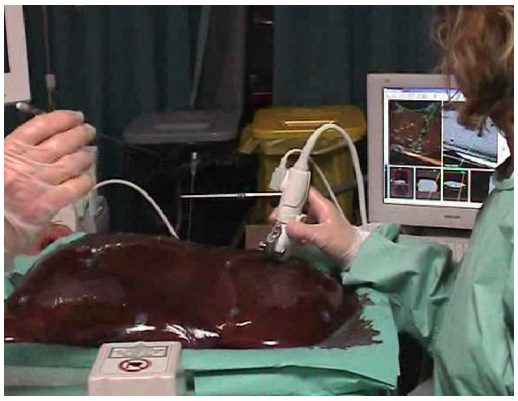

Fig.3

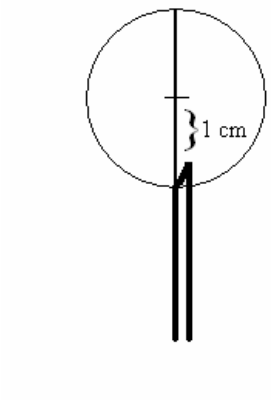

Fig.4

Fig. 2. The target is identified on the 'real-time' CT images during US assessment. The optimal biopsy route was chosen and a biopsy track was visualized.
Fig.3. A 21 G cytological needle 20 cm in length is used, together with the attached biopsy kit. In the back the matched US-CT image on the Virtual Navigator screen.
Fig.4. The tip of the trocar has to placed 1 cm from the centre of the intended ablation area (i.e. the pellet) for a 3 cm
Fig.5 (a,b). Multiplanar reconstructed CT images showing the distance between the pellet and the needle that was inserted under US-CT guidance

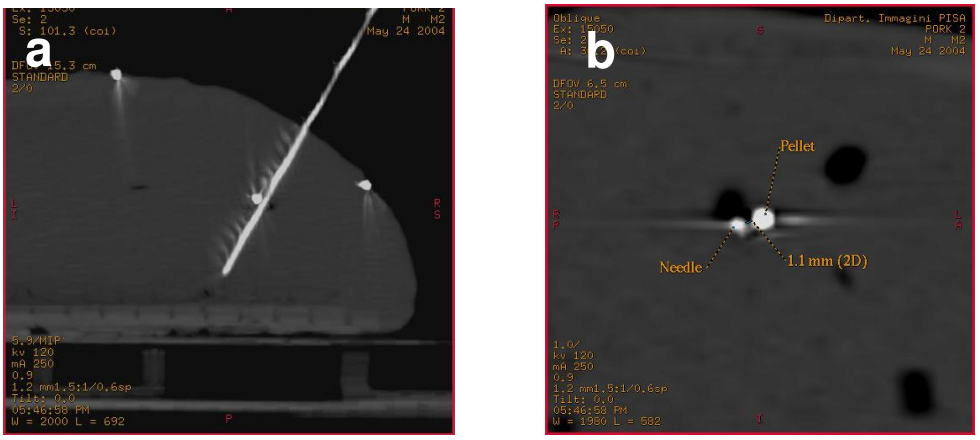

Fig 5 (a,b)

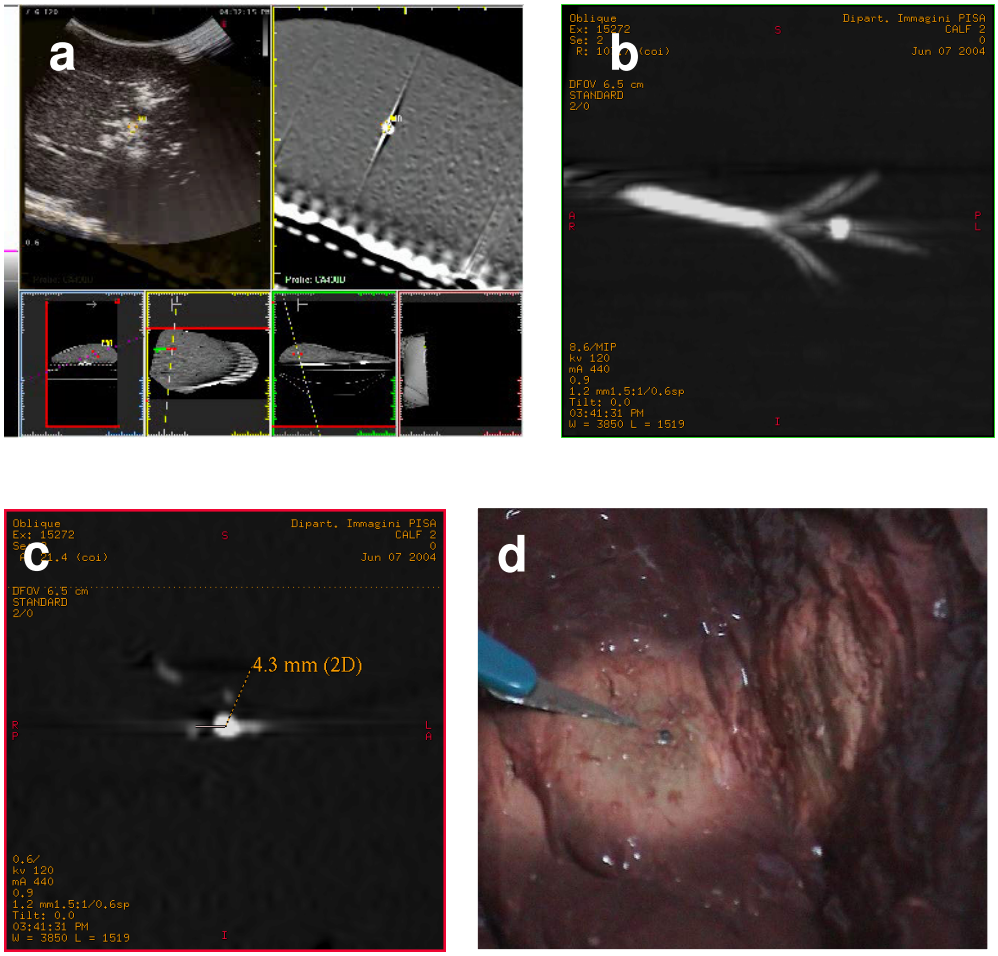

Fig. 6 (a-d). The target is identified on the 'real-time' CT images during US assessment and a 15 G RF multitined expandable electrode is inserted into the liver considering the target as the ideal centre of the ablation (a). Multiplanar reconstructed CT images show the relationship between the deployed hooks and the pellet (b) and the distance between the central tine and the pellet is calculated along a plane perpendicular to the electrode (c). After the dissection of the specimen the pellet is found unchanged in the center of the ablation zone (d)

DISCUSSION

US is a widely used tool for imaging guided procedures in the abdomen, especially in the liver. US is fast, easily available, allows real time imaging and is characterized by high natural contrast among parenchyma, lesions, and vessels. On the other hand, because of its high spatial resolution, good contrast, wide field of view, good reproducibility, and applicability to bony and air-filled structures, CT plays an important role especially in interventions which cannot be adequately guided by fluoroscopy or US [5-7]. However, in contrast to fluoroscopy and US, CT has been limited by the lack of real-time imaging so that many CT-guided abdominal interventions remain difficult or risky in several locations [8]. Moreover, the contrast resolution of baseline CT scan is low and many liver lesions are visible only during arterial and/or portal-venous phase of the dynamic study and not uncommonly needle localization under un-enhanced phase of image guidance is based on nearby anatomical landmarks [9]. The introduction of CT fluoroscopy allows real-time display of CT images with a markedly decreased patient radiation dose and total procedure time comparable with the use of conventional CT guidance [10]. Moreover new systems of breath-hold monitoring have been implemented and this could allow an easier access to mobile lesions [11]. However, despite marked improvements in procedure times compared with helical CT, CT fluoroscopy may still require 40% longer procedure times than US [12].

Therefore the ideal qualities of a targeting technique during image-guided liver procedures include clear delineation of the tumour(s) and the surrounding anatomy, coupled with real-time imaging and multiplanar and interactive capabilities [1]. Given the advantage of US guidance, it would be ideal if the procedure can be performed with real-time US matched with supplementary information from contrast enhanced CT or MR images. Numerous devices have been constructed to improve puncture accuracy for percutaneous radiological interventions and majority of these are based on CT [13-17]. Image fusion, the

process of aligning and superimposing images obtained using two different imaging modalities, is a rapidly evolving field of interest, with its own specific operational conditions [18-20].

To our knowledge this is the first report concerning the accuracy of targeting by using an image fusion system that matches real-time US and CT. In our feasibility study, we demonstrated a high and consistent level of matching accuracy with mean registration error 0.30 ± 0.01 cm and 0.29 ± 0.01 cm in the initial and second phase of the study, respectively. Apart from external markers, registration of CT data to intra-procedure US images using specific anatomical (e.g., portal and hepatic veins) and topographical (xiphoid sternum and umbilicus) landmarks can also be accomplished in real-time during US examination. For anatomical matching, accuracy in defining the specific point pairs in both CT and US images is necessary to obtain the best registration results.

We used a target that was undetectable at US and that was very small in size (1.5 mm). This ideally represents the situation of a tiny lesion that is visible only at CT. The navigation system represented therefore the only guidance for the procedures. By deciding to insert the needle only once for each targeting/ablation procedure, we reproduced the need of minimal invasiveness.

Excellent target accuracy was achieved in both phases of the study, with an acceptable mean needle to target distance of 1.9 ± 0.7 mm (range 0.84-3 mm) in phase I and a mean target-central tine distance of 3.9 ± 0.7 mm (range 2.94-5.14 mm) in phase II. Two our knowledge this is the first report about the accuracy of a fusion imaging system combining real time US with pre-acquired CT.

The main limitation of the study is the absence respiratory excursion and subject motion in this ex-vivo model. Either or both of these factors would introduce error but were not evaluated in our feasibility study. To extrapolate the utility in routine clinical practice, precise registration of CT volume images into the patient requires proper synchronisation with respect to the respiratory phase and arms' position during CT examination, and patient movement must be avoided. We appreciate that added procedure time may be required to achieve

accurate patient registration in some cases, but this may be offset by the time taken to perform needle localization and RF ablation of a lesion invisible or poorly conspicuous on routine unenhanced US or CT. Possible solutions for detection of patient movement would be the implementation of external electromagnetic position sensors to the patient's body. To target liver lesions that move during the breathing cycle, a breathing motion correction must be implemented. The solution could be based on methods used in radiation therapy, as well as on those used in positron emission tomography–CT image fusion [21-22].

Future advances include the automation of registration, which could further streamline clinical translation of such technologies. Miniaturization of internalized sensors for electromagnetic tracking of needles and ablation probes will have the ability to transform image guided needle-based procedures by providing real-time multi-modality feedback.

In conclusion real-time registration and fusion of pre-procedure CT volume images with intra-procedure US is feasible and accurate. For simple biopsies, an experienced interventionalist will not ask for such a guidance tool and, given the cost and availability, US and CT guidance will remain the "workhorses" for biopsy procedures. For lesion hardly visible at US or CT or for more complex procedures, such as thermal tumor ablations that require positioning of multiple applicators and puncture of multiple lesions, fusion imaging systems might be of help to reduce puncture risk and procedure time and to allow for more complete and radical therapy.

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