The role of image-fusion techniques for guidance of thermal liver ablation

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Learning objectives

- To **describe several fusion imaging modalities** (US/CEUS-CT, US-MRI, US-¹⁸FDG-PET/CT) and their use in guiding thermal ablation of liver tumours.

- Describe **technical aspects of the different fusion imaging modalities**.

- Recognize the **technical feasibility and efficacy of fusion imaging-guided thermal liver ablations of either totally undetectable or poorly visible liver tumours with ultrasound (US)**
Background

Over the last years, image-guided thermal ablation has assumed a growing and recognized role in the treatment of a series of abdominal tumours, especially small hepatocellular carcinoma (HCC). Currently, several different ablative techniques are available for image-guided ablations, including radiofrequency ablation (RFA) microwave ablation (MWA), cryoablation and laser ablation.

Precise and reliable imaging guidance is crucial for the safety and effectiveness of thermal ablations. Ultrasound (US) in particular shows several advantages in treatment guidance in abdominal applications, such as the real-time capability and the lack of ionizing radiation, and is the most commonly used guiding modality.

In cases of target lesions with poor conspicuity at US, contrast-enhanced US (CEUS) has been reported as a valuable aid and can also provide useful informations in treatment monitoring and in result assessment.

Nevertheless, other imaging methods, such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are widely used in the diagnosis of abdominal tumours and provide several advantages such as the possible application of contrast materials, an extended field of view (FOV) and increased conspicuity of some lesions.

Finally, a lot of tumours are nowadays diagnosed with functional imaging, such as Positron Emission Tomography (PET) used with a number of different radionuclides, which allow to identify the most vital part of a tumour, and to increase target detectability.

In order to be able of combining the advantages deriving from all these different imaging modalities without the need of multiple equipments, some companies developed a series of systems able to fuse together two or more imaging modalities, offering the so-called "fusion imaging (FI)" (Fig.1).

FI has been reported to be useful in all the different phases of an ablative procedure, from preoperative planning to lesion targeting, procedure monitoring and result assessment.
Fig. 1: Example of Ultrasonography and Computed tomography fusion with precise matching of liver margins and liver vessels.

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Findings and procedure details

In order to fuse two different imaging modalities, a variety of methods are available on the market, including optical systems (mostly used for surgical procedures), image-based (vascular interventions) or electromagnetic (EM) systems.

The last one is the most commonly used for image-guided thermal ablations and the vast majority of ultrasound companies offers nowadays US machines equipped with fusion imaging (FI) systems.

- The optical system (Fig.2) consists of a ray of laser or infrared light emitted or reflected from the instrument that is received by a camera at a fixed position overlooking the procedure area. Fiducial markers placed on the patient and the information from the visible part of the instrument are processed to achieve FI. An uninterrupted visual communication between the camera and instrument (line of sight) is needed for a proper functioning of an optical tracking system.

- The EM tracking system (Fig.3) consists of three main components: an EM field generator (that should be placed next to the patient), one or multiple position sensors (that can be applied to the US transducer, and to the patient) and the position sensor unit (incorporated inside the US machine). Additional position sensors can be applied to different devices, such as biopsy needles or thermal ablation devices. The EM field generator produces a magnetic field that disperses in a known quantity over distance. The positions sensors interact with the magnetic gradient and, as the US probe moves, the software installed on the US machine calculate the exact location of the position sensors and thus, their direction and position. Through this system, it is possible to achieve a precise fusion of US and other imaging modalities by simply identifying the same anatomical structure on the various imaging modalities or by applying external fiducial markers to the patient body at the time of reference imaging acquisition that can be then automatically recognized by the system at the time of the ablative procedure. The image fusion is practically performed through a "plane and point" manual registration. The experience of the operators determines the acquisition time that can vary consistently. The system displays a multiplanar reconstructed (MPR) image from the 3D dataset that corresponds to the real-time US image via a transformation matrix so that, as the US transducer is manually manipulated on the patient, the corresponding MPR image moves synchronously in real time.

In several cases, thermal ablation has been considered not feasible due to poor US visualization. The main causes of this are the presence of macronodular cirrhosis, the intrinsic poor conspicuity of the nodules, and the difficult location within the liver (such as in the liver dome, with poor acoustic window). Missing lesions that are not visible and
therefore not treatable with US or even CEUS guidance can be detected through FI with EM technology, and thus an increased number of nodules become treatable.

For instance, after the introduction of US/CECT FI in their clinical practice, Makino et al. reported an increase from 1.7% to 15.4% in the number of nodules with low visibility ablated, while maintaining unchanged the complete ablation rate.

Previously acquired CT scans can be successfully and easily fused with conventional US or CEUS. CT is the most used 2nd level imaging modality for the cirrhotic liver evaluation, enabling a correct evaluation of the nodules and their wash-in/wash out patterns. However, since the poor conspicuous lesions usually measure less than 2 cm and miss the typical dynamic pattern at the CT evaluation, contrast-enhanced MRI (CEMRI) might be the best imaging modality for the correct detection of the index lesion. In fact, FI combining US and the hepato-biliary phase of CEMRI with Gd-EOB-DTPA is more sensitive than conventional US or CEUS for detecting HCCs, especially for small (97% vs 66%) or atypical HCCs (95% vs 53%), and might be helpful in guiding thermal ablations (Fig.4; Fig.5). Lee et al. reported that FI with both CECT/CEMRI increased the conspicuity of the small nodes (<2cm) from 78.8% with US up to 90.5%. Bo et al. reported in a series of 70 lesions a conspicuity of 35.7% to the conventional US, of 70% with the fusion US-CECT/CEMRI and 95.7% with the fusion CEUS-CECT/CEMRI. Similarly, Dong et al., analyzing 49 nodes that were inconspicuous at conventional US, found an increased detection rate with CEUS of 42.9% and 95.9% with the CEUS-CECT/CEMRI fusion. Again, for small HCCs (diameter 1-2 cm), the detection rate using CEUS-CECT/CEMRI fusion (96.9%) was also significantly higher than CEUS (18.2%).

Regarding tumor ablation planning, despite literature data are still lacking, with virtual navigation it is also possible to draw the target tumour margins on the pre-acquired CT/MRI images that will be displayed on the fused real-time US images so that the operators can intuitively determine whether the target tumor and its ablative margins can be included by the avascular zone. During ablation, FI can be performed as in the preoperative planning. In case of patients being treated under general anesthesia, intraoperative FI-guided ablation might be even easier to perform due to more precise targeting through better respiratory control. Once precise fusion has been achieved, ablation can be performed with direct US visualization of the ablative device, or with the assistance of a virtual needle, that can be displayed on the US and/or on reference CT/MRI images (Fig.6).

This virtual needle might enhance correct targeting in cases of tumours with difficult locations when not only the lesion but also the tip of the ablative device is poorly visible (obese patients, interposed lung parenchyma, etc.). Once the needle has been positioned in the desired place, ablation is started, and gas formation during treatment can be overlayed on the reference images in order to initially understand the correct coverage of the desired tumour volume.
When the index lesion is targeted and ablation is performed, FI is further useful at least in two ways: intraoperatively and during follow-up.

Intraoperatively, as for lesion monitoring, FI can be used in order to precisely evaluate the ablation margins (at least 5 mm) and, in case, perform a supplementary ablation. The fusion can be performed 5-10 minutes after the first ablation (avoiding gas artefacts) overlapping CEUS with the pre-procedural image dataset to determine the ablated area and ablation margins (Fig.7). In the series by Li et al., 21.8% of HCC lesions with inadequate margins were finally completely ablated after FI-guided retreatment, improving the complete ablation rate at the first control. Being able to reflect the real-time micro-vascular blood perfusion of the ablation zone, CEUS can represent a useful mean of immediate treatment response assessment to indicate the complete ablation of tumour targets.

FI plays also a role in increasing the conspicuity of lesions to be treated also with High-intensity focused ultrasound (HIFU) (Fig.8;9;10). HIFU is a novel technique for thermal ablation, that can noninvasively deliver concentrated energy to locations deep in the human body and induce localized thermal coagulation responsible for irreversible cell damage without the need of a percutaneous applicator insertion.

Lastly, when liver lesions are inconspicuous even at CECT or MRI, and only or better visible with PET/CT, the fusion between US/CEUS and PET/CT may be of further help to enhance the detection rate of these lesions and to guide thermal ablation (Fig.11;12). Mauri et al. reported in a series of poorly visible or completely undetectable liver lesions at conventional imaging, a better correct targeting and a greater complete ablation rate of the lesions for the US-PET/CECT-guided group.
Fig. 2: System for virtual navigation system based on optical registration

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**Fig. 3:** Virtual navigation system for real-time US-CT/MRI image fusion. The system is made of an US scanner with a dedicated built-in hardware and software. An electromagnetic tracking system integrated in the workstation consists of a magnetic field transmitter (black arrow, A), fixed to the operation bed at the right upper quadrant of the abdomen, and two electromagnetic sensors, one applied to the convex ultrasound probe (white arrow, B), and one mounted on ablation applicator (arrowhead, C)

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Fig. 4: Pretreatment T1 MRI sequence shows a small hypo intense lesion of the liver (arrow).

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**Fig. 5:** Fusion imaging (ultrasonography and MRI) during thermal ablation treatment of the metastasis (needle: arrowhead, gas post treatment: cross). The location of the lesion (arrow) and of the portal vein (asterisk) shows the perfect overlap of the anatomical plans between Ultrasonography and MRI imaging modality.

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**Fig. 6:** (a) CT scan in arterial phase shows a hypervascular rounded mass (hepatocellular carcinoma) at segment VII, in cirrhotic liver. (b) With fusion imaging, after coregistration, on CT (right) the mass is manually demarcated (yellow line) and colored in blue. The corresponding lesion is visualized in the co-registered US scan (left). (c) Thanks to the application of an electromagnetic sensor to the hub of the microwave antenna used for
ablation, during the insertion into the target, the antenna is visible both on US (real device) (left) and on CT (virtual device, green parallel lines) (right). (d) Given the large size of the mass, multiple insertions are required for complete ablation. Following the first insertion, all the subsequent insertions are performed under the guidance of the "virtual needle" because the "cloud" of gas produced by the ablation prevents the visualization of the real device on US (left image). Based on pre-acquired data, the size of the volume of necrosis achievable with each insertion is represented as a green-colored sphere, overlapped by the fusion system over the blue-colored tumoral mass. When the overlapped green spheres cover the whole blue mass, the procedure is stopped. (e) After withdrawing the antenna, contrast-enhanced US is performed (left) and demonstrates an avascular volume of necrosis in the location of the mass. (f) Overlapping pretreatment CT over contrast-enhanced US in real time, it is seen that the volume of necrosis is definitely larger than the original tumor, as confirmed by contrast-enhanced CT acquired at 24 h after ablation (g)

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Fig. 7: Contrast enhanced Ultrasonography (CEUS) and T1 MRI imaging fusion after thermo ablation treatment of a 50 years old patient with colorectal metastasis for the result assessment. CEUS shows the lack of contrast enhancement in the treated lesion (arrow), in perfect anatomical overlap of the treated lesion on MRI imaging (arrow).

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Fig. 8: Computed tomography (CT) scan before treatment demonstrates a small hypodense nodule (arrow) close to the vena cava (asterisk).

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Fig. 9: Fusion imaging (ultrasonography and computed tomography) shows correspondence of the anatomical location of the lesion (arrow) as demonstrated by the same location of vessels between ultrasound and computed tomography (asterisk: vena cava, arrowhead: portal vein).

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**Fig. 10:** Computed tomography scan shows post treatment imaging of the lesion (arrow).

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**Fig. 11:** Fusion Ultrasonography and CT imaging that shows no lesion in the liver.
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**Fig. 12:** Fusion Ultrasonography and PET imaging that shows the liver lesion (arrow) allowing the thermal ablation treatment with ultrasonography guide.
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Conclusion

Thermal ablation has gained widespread attention and is increasingly used in a large variety of organs (primarily small, unresectable liver tumours).

Regardless of the organ and technique applied for ablation, precise image guidance is crucial in all the phases of image-guided ablations.

FI represents an ideal method to merge the advantages of the several available imaging modalities, overcoming their specific limitations. However, improvements are needed in order to ensure the best ablation results. Application of general anesthesia, image acquisition during the procedure, and advanced ventilation techniques, can further improve the results of FI, and help to promote a larger diffusion of it.

As technology makes progress, key limitation to image fusion in ablation such as CT or MRI images acquired days before the procedure, can be addressed. Cone-beam CT (CBCT), performed directly in the angio-room at the time of treatment, can provide a data set well suited to precise matching with real-time US images.

Overall, FI is a feasible and promising technique for tumours ablation, improving its technical feasibility and efficacy in terms of overall ablation accuracy, increased operator confidence and shortened procedural duration time.
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