ORIGINAL ARTICLE

Fusion Imaging in Neurosonology: Clinician's Questions, Technical Potentials and Applicability

Stephan J. Schreiber, Georgios Sakas, Velizar Kolev and Stefano de Beni

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Abstract

Purpose Ultrasound is a well established imaging technique with widespread use in diagnosis and treatment monitoring of neurological diseases. However, direct and exact comparison of results from conventional ultrasound with other frequently used diagnostic modalities like magnetic resonance imaging (MRI) or computed tomography (CT) is impaired by different field of views and non-identical imaging planes. A new technical approach - ultrasoud fusion imaging might help to overcome this problem.

Methods Fusion imaging is a technique which allows direct comparison of live ultrasound images with exactly corresponding images derived from pre-registered CT or MRI datasets. Different approaches for the matching procedure - manual or automated - can be applied for image fusion and movements of the patient are automatically corrected for.

Results The technique can widely be applied within the field of neurosonology. Clinical examples are given for its use in extra- and intracranial analysis of brain supplying arteries, intracranial parenchymal lesions but also for its use in peripheral nerve and muscle disease.

Conclusions Ultrasound fusion imaging is a promising technique which permits easy and exact matching between live ultrasound and CT or MRI image modalities, allowing for the first time a direct comparison between these techniques. This is a major step forward towards the facilitation of information exchange, reduction of interobserver variability and improvenment of image documentation.

Stephan J. Schreiber Charité University Hospital, Berlin, Germany

Georgios Sakas (⊠), Velizar Kolev MedCom GmbH, Darmstadt, Germany Tel : +49-6151-95147-13 / Fax : +49-6151-95147-20 E-mail : gsakas@medcom-online.de

Stefano de Beni Esaote spa, Genoa, Italy Keywords Ultrasound, Virtual navigation, Neurology, Image matching, Automated fusion

BACKGROUND

Diagnostic ultrasound is a technique well established in today's routine clinical practice. The questions to be answered by a neurosonological examination increased constantly over the years [1]. Typical examinations by extra- and intracranial insonation include diagnoses of stenoses or occlusion of the brain-supplying arteries and veins, vasomotor reactivity testing, search for cardiac right-left shunt, B-mode insonation of the brain parenchyma for assessment of structural lesions caused by elevated intracranial pressure, ischemia, hemorrhage, or Parkinson disease, diagnosis of vasculitis, muscle and peripheral nerve disease such as compression neuropathies, and others [1-3]. Above this, ultrasound assistance is requested for interventional guidance e.g. in central venous cannulation, ultrasound guided electromyography, botulinum toxine injection treatment or lumbar puncture, etc. [4-6].

There are several reasons for this increasing popularity of ultrasound in neurosonology: ultrasound is cheap and widely available, it can be utilized ad-hoc and without preparation. It is non-radiative and can therefore be used repeatedly on the same patient e.g. for monitoring purposes. Imaging is intuitive: every desired plane can be adjusted just by moving the hand. And last, the image quality is increasing constantly by technological progress of US equipment. However despite this great variety of already established applications, a number of ultrasound related problems are currently not well addressed:

1. While being an ideal bed-side technique, imaging has some limitations compared to the non-bedside techniques like computed tomography (CT) or magnetic resonance imaging (MRI): CT and MRI show a great anatomic clarity

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combined with standardized imaging planes (e.g. axial slices), easy to train and to re-identify. By ultrasound penetration of the scull is possible only at a few anatomical locations, a fact leading frequently to unconventional, tilted, non-parallel insonation planes making anatomical assignment of structures challenging. This particularly applies to insonation probes with sector fields, which cause additional image distortion. Today a specific hands-on training of the sonographer is required to compensate for this shortcoming.

2. With conventional ultrasound, comparison of specific structural findings with other diagnostic modalities such as CT, MRI or positron emission tomography (PET) is not possible, because the chosen ultrasound imaging planes hardly ever correspond with the classical axial, coronal or sagittal radiological imaging planes. On the other hand, comparison and correlation of findings between different diagnostic modalities is an essential requirement for diagnosis, planning, therapy and follow-up.

3. US is a "free hand" technique: considering the countless options in choosing an individual insonation plane, imaging of exactly the same region or point of interest during a reexamination and/or monitoring can be difficult or even impossible. However, repeated imaging of certain planes is essential for follow up, monitoring of treatment, progression or regression of disease in acute as well as chronic disease. Also comparability of results between different sonographers is equally important for a reliable diagnostic procedure.

All above mentioned problems cannot be solved using conventional ultrasound imaging. In this paper we present how the newly emerging fusion imaging technique may help to solve a majority of these problems.

FUSION IMAGING PROCEDURE

The general idea behind "fusion imaging" [7] is the combination of the real-time benefits resulting from ultrasound together with the anatomic clarity of images gathered by tomographic modalities such as CT, MRI or PET (or a combination of these) [8-13]. Our system shows thereby to every live US image a corresponding, co-register side-to-side plane extracted in real time from a tomographic modality. The idea is that the anatomic clarity of the tomographic images, familiar to the examiner due to his year-long training, effectively assists understanding the content of the sometimes more difficult to interpret US images. By overlaying of the two images, borders, shape and location of anatomic structures can be localized in the US image and by the time their interpretation becomes more and more familiar, resulting in a steep learning curve.

The first step is to scan the patient with the reference



Fig. 1. The navigated neurosonography environment.

modality (typically MRI). MRI scans are transferred to the navigation system in digital imaging and communications in medicine (DICOM) format using disc, stick or LAN connection. The Virtual Navigation unit processes every slice, taking into account the (sometimes unequal) slice thickness and spacing, and generates a homogeneous 3D volume out of them, showing the three orthogonal planes.

Technically the system employs an Esaote US scanner integrated with the MedCom Navigation unit (Fig. 1). The US system is equipped with the Esaote PA240 probe (2), a variable band phased array with operating bandwidth of $4 \sim$ 1 MHz and able to provide images from the scull interior. The Esaote scanner provides the US image and its characteristics such as the spatial dimension, orientation and the probe's fields of view.

The fusion imaging system called "Virtual Navigator" has been developed by MedCom GmbH and is integrated within the Esaote scanner. An electromagnetic tracking system, composed by a transmitter (1) and a small receiver mounted on the US probe (2), measures the position and orientation of the US probe in relation to the transmitter over 100x per second. This tracking system generates an electromagnetic field, which is strongest at the transmitter site and attenuates with distance. The total operative range is 70 cm, however since the highest accuracy is achievable close to the transmitter, the transmitter is placed ~ 20 cm far from the head of the examined subject. The electromagnetic tracker works even if an object, body, person, medical tool etc., is located between the transmitter and the receiver blocking the direct line-of-sight and it can be easily placed in any environment, furthermore the cost is acceptable. A disadvantage of the magnetic principle is its sensitivity concerning certain types

of massive metallic objects (iron, aluminum etc.) close to the receiver or between receiver and transmitter. However it has been found during the clinical tests that avoiding the presence of large metallic objects within the critical area of the examination environment can be achieved without affecting the clinical routine in noticeable way.

A second small receiver is located on the patient's head (3). This additional tracker follows the movement of the head during the examination and enables thus a "virtual immobilization" of the patient: in case of patient movement the new position is considered and the registration adapted accordingly in real time, resulting on the screen in a seemingly unmoved patient.

Registration between patient anatomy and its tomographic data can be performed either manually or by a fully automated method. In the manual case [14-19] the registration procedure of the MRI volume and the real-time US scan consists of two phases: an initial registration and a fine tuning. The initial rigid registration is based on external anatomical landmarks correspondences: several (typically eight) anatomical landmarks selected on the scull surface (tip of the nose and glabella on the midline; lateral canthus, tragus, ear attachment bilaterally) can be identified on the MRI scan and tipped also on the head of the patient (Fig. 1) by using the 3D pointer (4).

After this initial registration the system extracts in real time an oblique MRI slice at the location and orientation parallel to the US image, and both images are displayed on the screen. Overlapping of the MRI and US image enables quick and intuitive test of the registration accuracy (Figs. 4, 6, 7) by checking for misalignment of major anatomical

structures such as ventricles, vessels, mid-brain, dural structures between the MRI image and the real-time US image [20-23]. If a displacement is observed, the error might be corrected in two ways:

- In-plane correction: If the same characteristic landmark is visible on both images, freeze the displayed US and MRI images on the screen, then drag/shift/rotate one image with the mouse to the correct position over the other
- Out-of-plane correction: if no common landmarks are visible, select one or more clearly visible anatomic landmark(s) on one of the modalities, freeze said image and move the probe until the other (still moving) modality displays the same information as the frozen one; now click on the same anatomic landmark in both images thus matching both modalities.

In addition to the manual procedure we developed also a fully automatic method based on the identification of corresponding vessels structures in tomography and US. Vessels in CT or MRI are recognized based on their gray level and segmented by an adapted region growing algorithm combining grey value, cylindrical shape proximity and other constrains such as line-likeness and maximal volume. Then, an US three-dimensional Color Doppler volume of the brain vascular tree (Fig. 3) is acquired in the same region of interest. Vascular structures are highlighted by color whereas parenchyma shows only a black and white structure. The employed Esaote US scanner provides separate channels for B/W and color information making the task of vessel segmentation even more robust.

The automatic registration matched the volumes containing



Fig. 2. Automatic registration based on vessel structures.



Fig. 3. Top left: extracranial longitudinal insonation of a high-grade carotid stenosis. Top right: corresponding matched CT angiographic image.



Fig. 4. Top row: transtemporal insonation, axial imaging plane, and corresponding MRI and fusion image. Left: B-mode image of the midbrain-plane. Middle: corresponding T1-weighted post contrast MRI image. Right: Overlay image of both imaging modalities. Middle row: 3D-visualization of the chosen imaging plane and partial image of the 3D-surface rendering derived from the MRI dataset. Bottom row: Left: color-mode imaging of the basal cerebral arteries in excellent correspondence with the hypodense flow void signals of the MRI (right). Midbrain delineation = white arrows. MCA = middle cerebral artery, ACA = anterior cerebral artery, PCA = posterior cerebral artery.

only the extracted, filtered and resampled vessels, through a downhill simplex algorithm, which maximizes the common part of the vessel trees. Our approach converges within less than 5 seconds and works robustly even when only fragments of the vessels have been identified in the US scan.

APPLICATIONS IN NEUROSONOLOGY

Neck and brain

Extracranial insonation

In patients with vascular risk constellation or ischemic stroke, ultrasound of the brain-supplying arteries is a standard diagnostic procedure. Insonation conditions are usually good. However, sometimes orientation might be difficult in vessel elongation or vessel wall pathology with calcified plaques. Re-visiting identical locations of insonation (e.g. for grading of a stenosis) in a long-term follow up is a challenge for the sonographer. The Virtual Navigator solves this task by storing the examination location as US image registered to the tomographic scan: in the follow-up, patients are reregistered with their (initial) tomographies and the desired location can be re-visited easily. Fig. 3 demonstrates the application of the fusion imaging technique in a patient with left-sided carotid stenosis. Note the blue-cross marker defining matched locations in both data sets. Bottom row images: 3D-visualization of the chosen imaging plane and partial image of the 3D-surface rendering derived from computed tomography angiography (CTA).

Transcranial insonation

A great number of ultrasound studies in neurology are transcranial studies of vessels and parenchyma through the temporal or transforaminal bone window. As these windows are small, insonation is like "looking through a key-hole" and the resulting imaging planes do not resemble the classical axial, sagital or coronal plane. Instead, they are unconventionally oblique, which might impair the identification of insonated structures. Fig. 4 gives examples for a typical transcranial insonation plane. See the butterfly-shaped midbrain (red arrows) and the surrounding hyperechogenic basal cisterns on the top-left B-mode image. On the top-right the overlay image demonstrates excellent congruence of ultrasound and MR scans.

In case of specific lesions, e.g. a tumor, ischemia or hemorrhage, such structures can be delineated in the CT or MRI modality and then be projected into the live ultrasound image for direct comparison. This approach is the precondition for re-visiting of identical regions for follow-up over time. Fig. 5 gives an example of an intracranial tumor in comparison between MRI and transcranial ultrasound.



Fig. 5. Top row: transtemporal insonation, axial imaging plane, corresponding MRI showing a left-sided meningioma. Note the bluecoded delineation of the lesion in the MRI and the ultrasound image. Top left: Harmonic imaging mode in the phase of contrast bolus arrival (white box = non contrast enhanced image). Note the contrast filling exactly within the delineated borders of the hyperperfused meningioma. Top right: corresponding T1-post contrast MRI, also demonstrating contrast enhancement. Bottom row: 3D-visualization of the chosen imaging plane and partial image of the 3D-surface rendering derived from the MRI.



Fig. 6. Top and middle row: Cross-sectional insonation of the left lower leg, corresponding MRI and fusion image. Top left: B-mode image of the tibial bone (white arrows) and hyperechogenic Musculus tibialis anterior (red arrows). Note the atypical bright grey B-mode aspect of the muscle. Top middle: corresponding cross-sectional MRI image demonstration almost white muscle aspect. Top right: overlay image of both imaging modalities, demonstrating excellent congruence of ultrasound and MR image. Middle left: ultrasound position turned more laterally visualizing a greater area of the muscle parenchyma – note the continuing excellent matching.



Fig. 7. Top row: Cross-sectional insonation of the left upper leg in a patient with a neurofibromatosis and corresponding MRI. Top left: ultrasound image with delineation of the femoral bone (white arrows) and a large neurofibroma (red arrows). Middle left: B-mode image of the same lesion centered to the image. Middle: corresponding cross-sectional MRI image. Middle right: overlay image of both imaging modalities, demonstrating good congruence of ultrasound and MR image.

Muscles and nerves

Muscle insonation

Muscle diseases, especially the wide variety of either myogenic or neurogenic myopathies, are today a diagnostic challenge for the clinical neurologist. Established diagnostic approaches are electrophysiological testing like neurography and myography, laboratory analysis of blood samples, and imaging by MRI. In a large number of patients the above diagnostic steps are not sufficient to finalize the diagnosis and a muscle biopsy, based on the pathology seen on MRI, is necessary. However, localization of an affected muscle part for correctly biopsy it is challenging for the surgeon. Ultrasound of peripheral muscles has already been studied some years ago but has not become a major diagnostic step as image sensitivity seems low and orientation frequently doubtful. Combining MRI and ultrasound by using the fusion imaging technique is intuitive and helpful to identify affected muscles and to mark optimal places for diagnostic biopsy. Fig. 6 illustrates the fusion imaging approach in the lower leg of a patient with peripheral muscle disease.

Nerve insonation

In recent years and with the development of high-frequency ultrasound probes with subsequent drastic improvement of B-mode image quality, ultrasound of peripheral nerves has increasingly being used to gather structural information about nerves and peripheral nerve disease. Frequently questions prior to interventions (e.g. evaluate for decompressive surgery of peripheral nerves) or postoperative assessments (e.g. after trauma) have to be answered. CT and MRI are lacking so far the necessary spatial resolution to evaluate these very fine structures in the needed spatial resolution detail. Fig. 7 illustrates upper leg imaging of a patient with a neurofibromatosis and preoperative neurofibroma assessment.

SUMMARY

Fusion imaging is a promising technique which allows easy correlation of live ultrasound and pre-acquired tomographies (MRI, CT, PET etc.). Navigating and interpreting of images, structures and anatomy is then becoming intuitive and highly ergonomic. The application of this technique facilitates identification of insonated structures as direct and simultaneous comparison with the second imaging modality is available. Unconventional imaging planes regardless of the insonated region are no longer a problem, as the multimodal imaging approach aids the investigator and helps to develop an understanding for the three-dimensional structures. This is particularly true for the use of non-linear ultrasound probes, despite the fact that image distortions caused by probe configuration are not yet corrected.

The overlay technique in combination with additional delineation of lesions or regions, together with its simultaneous visualization on ultrasound and MRI or CT, is an approach to mark and identify a specific point or imaging plane. As this approach can be repeated in successive ultrasound studies the technique permits for the first time the opportunity of ultrasound image comparison at identical locations, provided that the matching process is performed in identical manners. Subsequently, this is a major step forward towards the improvement of image documentation, of follow-up studies over time and towards the reduction of interobserver variability.

Result of the above illustrated technical development and its advantages an increasing number of reports on first clinical applications within the field of neurosonology have recently been published [23-26].

CONFLICT OF INTEREST STATEMENTS

Schreiber SJ has been supported by Esaote by lending of a research Mylab Twice ultrasound and virtual navigator system. Sakas G is MEDCOM CEO. Kolev V is a MEDCOM employee. De Beni S is an Esaote employee.

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