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Ultrasound Image Fusion: A New Strategy to Reduce X-Ray Exposure During Image Guided Pain Therapies

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1. Introduction

Many pain procedures cannot reliably be performed with a blind technique. Thus, imaging guidance is frequently mandatory, above all when the region of interest is deep and/or difficult to reach. In recent years new imaging techniques have been developed to improve diagnosis and to display greater anatomical details. Both Radiology and Pain Therapy have developed new and more accurate techniques in interventional pain, linked to a better understanding of pathophysiology and mechanisms of pain.

There are many important anesthetic blocks performed under ultrasound guidance, but our experience is mainly based on pudendal nerve and sacro-iliac joint infiltration.

2. Pudendal nerve

Chronic perineal pain syndrome, due to pudendal nerve impingement, has a specific etiology and taxonomy among other possible pain sources in the pelvic and perineal area. Typically patients present uni or bilateral pain in the perineum, which may be anterior (urogenital), posterior (anal) or mixed, with a history of local treatments failure (proctologic, urologic or gynecologic). Postural nature of the pain, exacerbated, if not entirely provoked, by the seated position, led to a therapeutic strategy based on peri-truncal anesthetic blocks (Robert et al., 1998). Chronic pelvic pain was estimated to affect approximately 15–20% of women aged 18–50 (Mathias et al., 1996). On the other hand, the prevalence in men is near 8% considering urological examinations, but only 1% during primary care consultations (Schaeffer, 2004). The pudendal nerve, a mixed (sensory and motor) nerve, supplies the anus, the urethral sphincters, the pelvic floor and the perineum, furthermore it provides for genital sensitivity. It arises from anterior rami of the second, third, and fourth sacral nerves on the ventral aspect of the piriformis muscle in the pelvic cavity and crosses the gluteal region, passing through the greater ischiatic foramen, into the infrapiriformis canal, accompanied by its artery. It is also surrounded by veins with plexiform appearance (pudendal neurovascular bundle). This bundle courses around the sacrospinous ligament just before the latter's attachment to the ischial spine, enters the perineum through the lesser ischiatic foramen and courses through the ischiorectal fossa and then through the pudendal

(Alcock's) canal. The Alcock's canal is the fascia tunnel formed by the duplication of the obturator internus muscle under the plane of the levator ani muscle on the lateral wall of the ischiorectal fossa. Subsequently, the pudendal nerve splits into three terminal branches: the dorsal nerve of the penis (or clitoris), the inferior rectal nerve, and the perineal nerve, providing the sensory branches to the skin of the penis (or clitoris), the perianal area, and the posterior surface of the scrotum or labia majora. It also innervates the external anal sphincter (inferior rectal nerve) and deep muscles of the urogenital triangle (perineal nerve) (Labat et al., 2008; Lefaucheur et al., 2007). Pudendal nerve impingements are possible in its proximal segment in the pinch between the sacrospinous and sacrotuberous ligaments at the ischial spine and when it crosses the inner border of the sacrotuberous ligament, which is thickened at the beginning of the falciform process. Another possible entrapment site may occur in the Alcock's canal as a result of a thickening of the obturator internus muscle fascia. Finally the pudendal artery may describe perineural curves or constrict the nerve trunk with its collateral branches. The vessels, often tortuous and dilated, narrow nerve's components within the vascular sheath (Robert et al., 1998; Lefaucheur et al., 2007; Labat et al., 1990).

Then, nerve decompression is made with different therapeutic conservative or surgical strategies (Robert et al., 2004; Amarenco et al., 1991). Peripheral nerve blocks approach was first described in 1908 (Benson and Griffis, 2005) and it is actually used by pain therapists. There are many different ways of placing needle: by a fluoroscopic, electroneuromyography (ENMG), computed tomography (CT) or ultrasound (US) guide. Pudendal nerve block is usually made with conventional fluoroscopic guidance with placement of the needle tip near the apex of the iliac crest (Calvillo et al., 2000) but fluoroscopy is unable to visualize the pudendal nerve in the anatomical plane formed by the sacrospinous and sacrotuberous ligament (interligamentous plane). Moreover, this technique exposed to ionizing radiations both patient and physician. CT guidance, first used 1999 (Thoumas et al., 1999), is also well established and documented (Fanucci et al., 2009; Robert et al., 2005; McDonald and Spigos, 2000). Using CT it is easy to recognize ischial spine, sacrospinous and sacrotuberous ligaments and pudendal bundle. Then, we can not only place needle tip in the interligamentous space (between the sacrospinous and sacrotuberous ligaments, as close as possible to the caudal portion of the ischial spine) but it is also possible to inject pudendal nerve at the entrance of Alcock's canal (a scan, at the level of the pubic symphysis, allows to identify pudendal bundle on the medial aspect of the obturator internus) (Fanucci et al., 2009). Despite all these benefits, this technique is performed without real-time visual control, and it leads to risks of unintended puncture of adjacent vessels. Ultrasonography allows the direct visualization of the ischial spine, sacrospinous and sacrotuberous ligament. Moreover color-Doppler improves pudendal artery's visualization. In a feasibility study (Rofaeel et al., 2008), it was shown that the pudendal nerve could be clearly visualized only in 12% of the patients. Pudendal nerve shows a diameter more or less between 4 mm to 6 mm (Mahakkanukrauh et al., 2005; Gruber et al., 2001; O'Bichere et al., 2000). All the structures of this size are hardly detected by US at a depth of 5.2-11.1 cm. Furthermore, the depth of the ischial spine from the cutaneous plane is usually more than 7 cm and in 30-40% of the cases, the pudendal nerve shows anatomical variants making the nerve visualization more difficult, especially when the pudendal nerve has dense or fatty tissue near itself, with a possible failure of the procedure. For all these reasons US is usually combined with intraoperative fluoroscopy with a concordance of the two methods in 82% of the

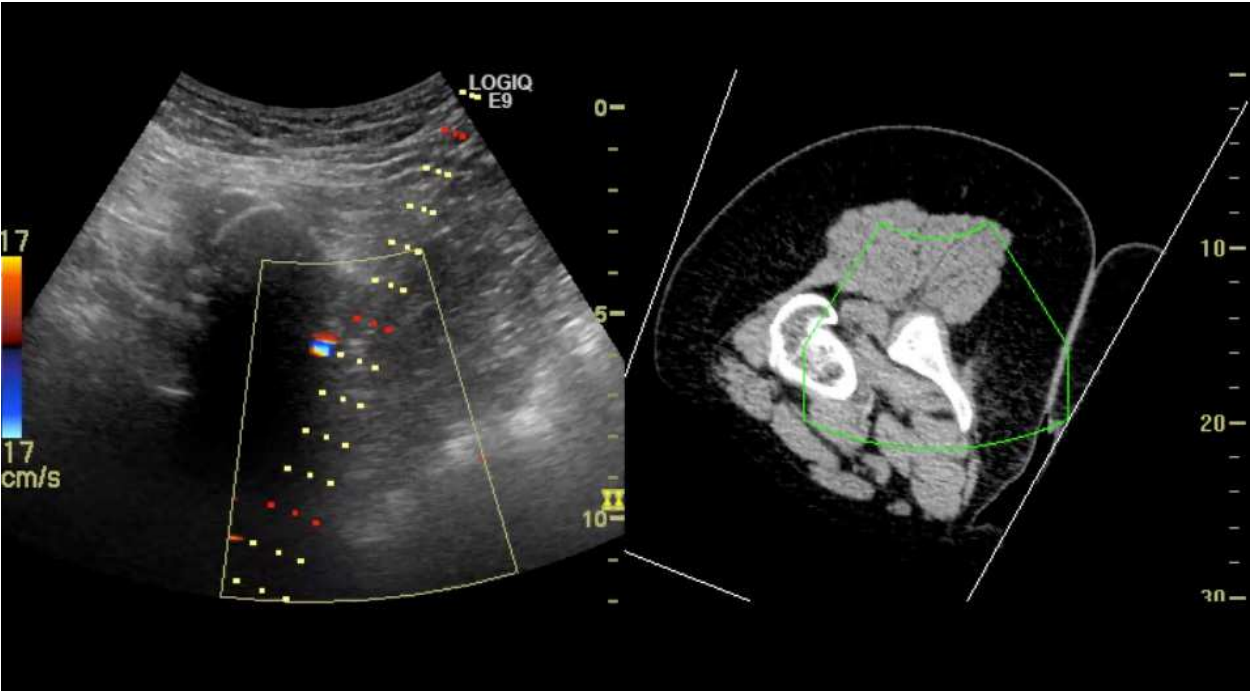


Fig. 1-a. the patient is in prone position. Fusion imaging of left side Alcock canal, pudendal artery (landmark for pudendal nerve) is visible in US side by color Doppler signal medially to ischium bone

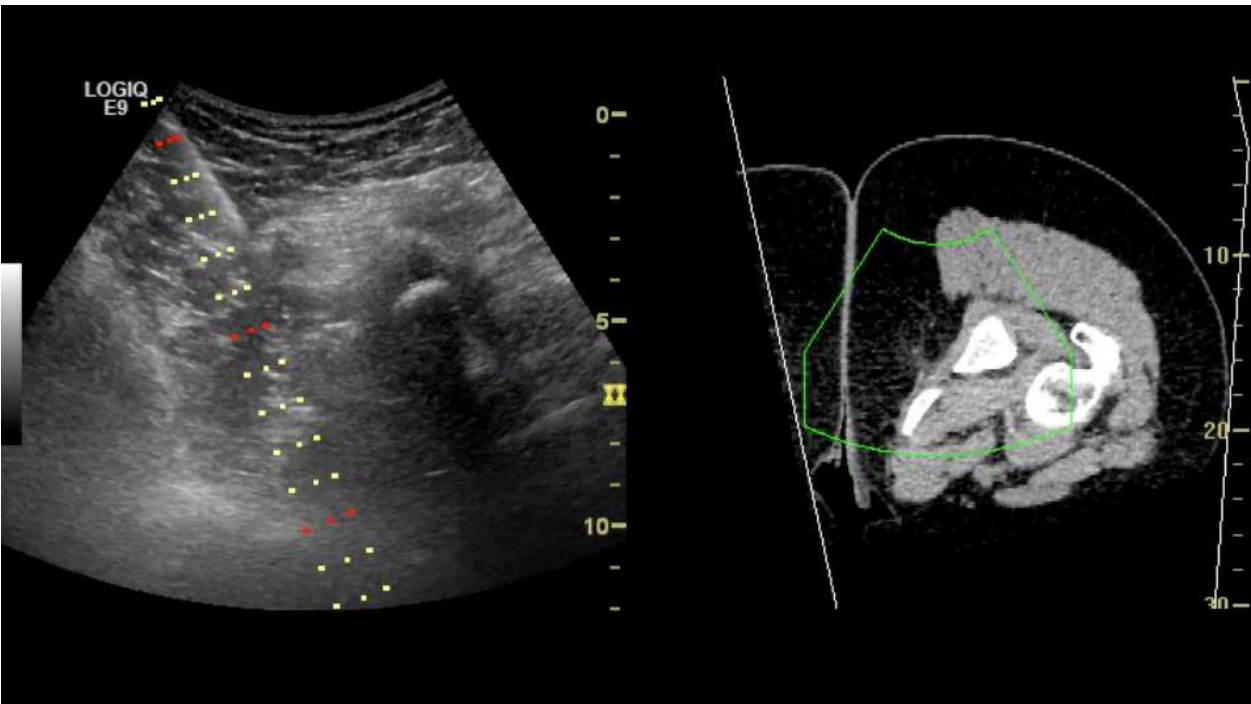


Fig. 1-b. Fusion imaging of right side Alcock canal. The spread of anesthetic solution is visible along the needle tract

procedures (Mahakkanukrauh et al, 2005; Gruber et al., 2001). Some authors describe an easier nerve visualization using a supplementary injection of quiescent solution, as reverse contrast, which should outline nerve's borders (Gray, 2006). Moreover US guidance ensures real-time needle advancement and confirmation of injection spread within the interligamentous plane (Peng and Tumber, 2008). Ultrasound guided block is a simple and reproducible approach avoiding ionizing radiations (Abdi et al; 2004).

3. The sacro-iliac joint

The sacro-iliac joint is a potential source of low back pain and/or buttock pain with or without lower extremity pain. Sacroiliac joint pain may be the result of direct trauma, unidirectional pelvic shear, repetitive and torsional forces, inflammation, or idiopathic onset. The prevalence of sacroiliac joint pain is estimated to range between 10% and 38% with 95% confidence intervals of 0% – 51% (Manchikanti 2009). It's a diarthrodial synovial joint but only the anterior portion and inferior one third of the SI joint is a true synovial joint, because of an absent or rudimentary posterior capsule, the SI ligamentous structure is more extensive dorsally, functioning as a connecting band between the sacrum and ilia. The anterior portion of the sacroiliac joint likely receives its major innervation from posterior rami of the L1-S2 roots but may also receive innervation from the obturator nerve, superior gluteal nerve, and lumbosacral trunk. The posterior aspect of the joint is supplied by the posterior rami of L4-S3, with major contribution from S1 and S2.

For this complex anatomy a clinically guided injection results actually intra-articular only in few cases. Particularly Rosenberg et al. demonstrated a success rate of 22%.

An image guide is required to reach the joint. Since 2000 Dussalt et al proved a fluoroscopy guide as a safe and rapid procedure. They rotated the fluoroscopic tube and reached the posterior aspect of the caudal end of the joint in 97% of the injections. Many authors used a CT guide with subsequent good results.

However radiation exposure under fluoroscopy guided SI joint injection ranges from 12-30 mGy/minute for the skin and 0.1-0.6 mGy/minute for the gonads, and using a CT guidance it may vary from 10 to 30 mGy/minute for the skin. Moreover ionizing radiation exposure leads to stochastic genetic and carcinogenic effects. Some authors have suggested using magnetic resonance (MR) imaging guidance to achieve intra-articular rates of up to 97% (Pereira, 2000). An MRI based procedure was found effective and safe, with the additional advantage to detect bone edema and others inflammatory signs. Even if both CT and MRI imaging are useful technique with an high contrast and spatial resolution, they takes too long with a cumbersome equipment. For all these reasons and to avoid radiation exposure Pekkaali et al. tried to perform SI joint injection using a sonographic guidance. They obtained a successful intra-articular injection rate of 60% for the first half of the procedures and about 93.5% in the last half. Pekkaali, Klauser, Migliore et al. showed that sonographically guided technique may be a valuable alternative in SI joint interventions, safe, rapid and reproducible, with the possibility to detect inflammatory signs using color-Doppler even if the result depends on radiologist's training. However a successful intra-articular injection using a sonographic guide depends not only on the radiologist experience in US performed anesthetic block, but also on the kind of patients and on the disease staging. In fact it's well known that patient's body mass index influences sonographic scans, like the presence of bone spurs or articular space narrowing, due to the pathology itself.

For all these reasons both these anesthetic procedures requires a new strategy in the guidance of the block itself, to reach the region of interest avoiding radiation exposures, like fusion imaging technique.

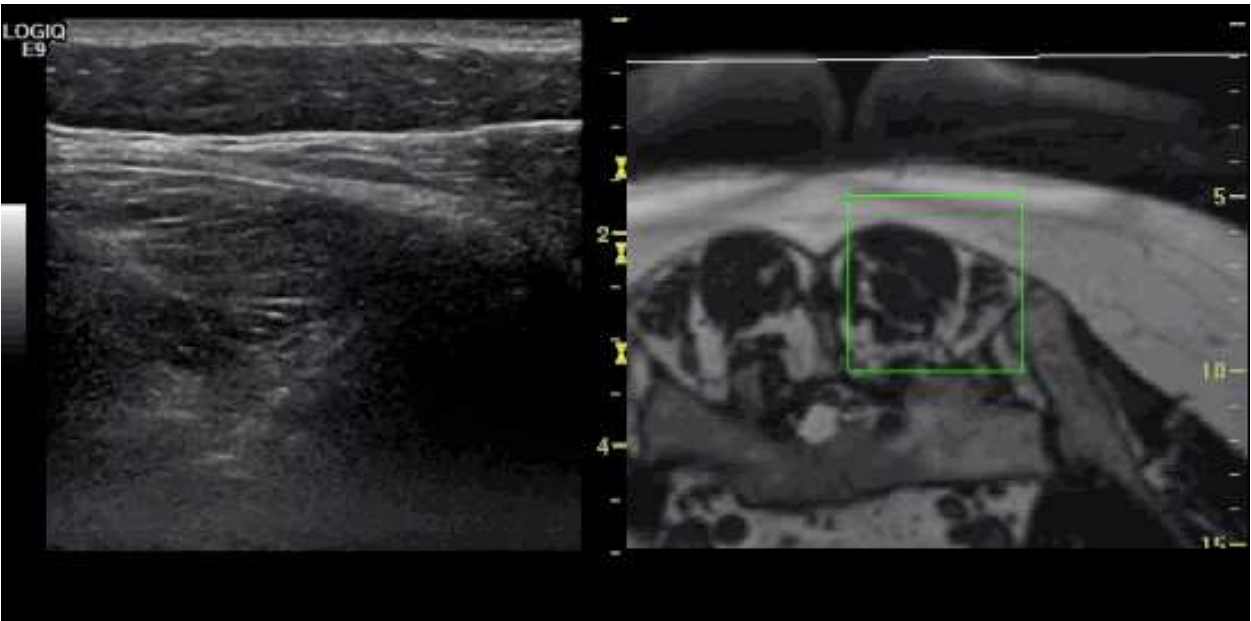


Fig. 2-a. Fusion imaging of right sacroiliac joint at second sacral foramen
Courtesy of Massimo Allegri, Pain Therapy Unit Policlinico S. Matteo Pavia



Fig. 2-b. the needle position is easily visible on the US side of Fusion Imaging. The needle tip is approaching the sacroiliac joint
Courtesy of Massimo Allegri, Pain Therapy Unit Policlinico S. Matteo Pavia

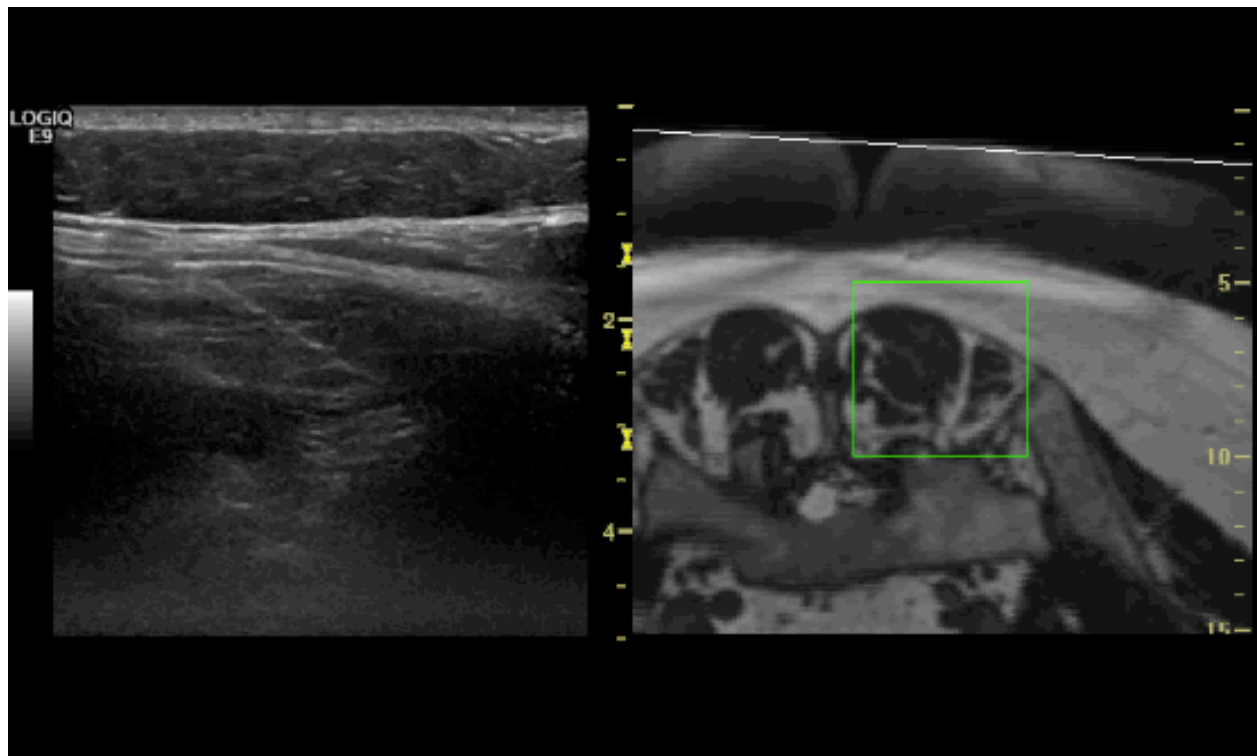


Fig. 2-c. the needle position is easily visible on the US side of Fusion Imaging. The needle tip is approaching the sacroiliac joint

Courtesy of Massimo Allegri, Pain Therapy Unit Policlinico S. Matteo Pavia

4. Fusion imaging

Fusion system can simultaneously show both ultrasound imaging with previous magnetic resonance (MR) and CT study. The basic concept of imaging fusion depends on the idea that an MR/CT study creates a 3D data set that represents the patient's anatomy. The 3D DICOM data set can be stored in any convenient imaging network location. On the other hand, US is the real-time modality, mostly used, that allows to use a feature called "Volume Navigation" to virtually project the patient's previous statics MR/CT data into the space where the clinician is performing a live, real-time, ultrasound. As the operator scans, the ultrasound system shows both the real-time ultrasound and the corresponding slice through the previous MR/CT 3D data. This is a real time reconstruction of an arbitrary slice through the MR/CT 3D data set morphed, with US data into a single unit so that the radiologist or pain therapist can intuitively use both imaging modalities simultaneously to provide diagnosis and treatment guidance. The images are presented in several formats. When presented side by side, the user can see the live ultrasound on one side of the display and the corresponding MR/CT on the other side (split screen image). Similarly when presented side by side the zoom factor of the MR/CT image and US should be varied simultaneously. In this view, the user can see not only the small live field of view (FOV) of ultrasound but also the rest of the MR/CT image that lies outside of the ultrasound scanning area but in the same plane of view. That adds the benefit of the MR/CT's wide FOV to the comparably narrow scope of ultrasound image. The images can also be presented in a mixed mode with MR/CT and US fused data from both modalities. Fusion imaging allows recording CT or

MRI data with US images in real time through an electromagnetic transmitter placed near the patient with two sensors closely bound to the probe. All these components are linked to a GPS system responsible to track the position of the ultrasound probe and to correlate with CT/MRI 3D data set. The critical phase of this procedure is the intermodality registration, involving the precise identification of multiple selected anatomical landmarks of the same patient on the different imaging modalities. Fusion imaging advantages are: 1. Ultrasound suffers from a relatively narrow FOV. MR/CT, by contrast, has an optimal contrast resolution and a wide FOV but lacks real time. Furthermore

- Ultrasound is well suited for many interventional procedures because of its real-time imaging.
- The fusion of CT/MRI and US allows using Color- Doppler or CEUS superimposed with CT/MRI.
- Fusing the images from different modalities could help to avoid multiple exposures to ionizing radiations, improving costs, and quality.
- To date, fusion imaging has been used for many diagnostic and interventional applications.

The first experiences in fusion imaging were carried out on liver imaging, because both biopsy or ablation therapy (radiofrequency) should require an imaging help.

Crocetti's group was the first to test the feasibility of fusion imaging, matching volumetric CT data of the calf livers containing internal targets, which simulated liver lesions, with real time US. The authors tried to reach each target using fusion imaging guidance and finally to perform a radiofrequency ablation. Their protocol consisted of various steps, but the most important is the registration time, during which ultrasound live examination was mixed with the previous CT scan, using radio-opaque markers applied to the calf liver capsule. Every marker was put down with a system of numbering. However during the procedure the authors used others target points (anatomic marker) to confirm the real concordance between both the modalities, such as portal vein. They found an high and consistent level of matching accuracy.

They used very small (1.5 mm) US undetectable target, reproducing a tiny lesion visible only at CT. The navigation system represented therefore the only guidance for the procedures.

However an important limitation of this study was the absence of breath and the absence of a real patient with a subsequent "lesion movement". They suggested solving this problem with the implementation of external electromagnetic position sensors, to patient body and using a breathing motion correction.

Crocetti however proved that fusion imaging could improve liver lesion interventional procedures, with a new possibility for all that lesions that are difficult to see on US B-mode scan.

At the present time, fusion imaging is realized with a new feature called volume navigation technology, which allows to mix US scan with CT/MRI DICOM data, and which uses a magnetic sensor to locate the probe position. Particularly the transmitter is fixed to, or near to, the patient's table as close as possible to the region of interest.

So the registration time becomes very important, like the choice of the target points, and it affects the success of the procedure. There is another important study carried out to analyze the accuracy of fusion imaging between CT and US to guide liver interventional procedures, according to several variables, that can impact the accuracy of this technique in clinical

conditions. Hakime et al. measured the different spatial locations of an established target lesion between virtual CT and US examination in real time.

They used some anatomical intra-hepatic and extra-hepatic landmarks with the help of some non-anatomical landmarks (cysts/calcification). On CT scan, they preferred to use portal phase during which tumor is much more visible such as the portal vein, an important anatomical target point. In this study the authors analyzed also breathing influence, that lead to a global distortion along the three axes, and they suggested to display respiration cycle, that could be helpful in non-anesthetized patients.

They found a greater mismatch for anterior-posterior axis versus the lateral one, maybe due to the pressure applied with the probe.

Another important result of this study is the variation in accuracy when patient was under general anesthesia, or when CT scan was performed several days before of the procedure. Both these conditions lead to more errors during registration time, probably because the patients took a different position with a subsequent distortion of the volume body. Moreover for patients under anesthesia was impossible to repeat the same apnea conditions. In liver pathology diagnosis plays an important rule too. In fact in literature there are some reports using fusion imaging to optimize liver involvement. For example Jung's group first tested liver lesions characterization, vascularisation and perfusion using fusion imaging. Particularly they used contrast-enhanced US mixed with contrast-enhanced MD-CT in seventeen cases and with contrast-enhanced MRI in three cases. They preferred an arterial phase during the examination of Hepatocellular Carcinoma and of neuroendocrine tumors, a portal phase for the metastasis (above all for colo-rectal ones) and finally, for hemangiomas and focal nodular hyperplasia, the phase in which the tumors could be easily visualized. As target points they used above all vascular structure, both artery and veins. An additional registration was done when a lesion was visualized, particularly providing an adjustment of the lesion size.

They found a better characterization of liver lesions by matching different contrast-enhanced modalities, because this new feature could employ the advantages of the different imaging methods. Using an additional registration they marked even small lesions or they reached also a better characterization in cirrhotic livers, where important liver structure changes, due to the pathology itself, influenced a correct diagnosis. Even if one important limitation of this study was the number of cases, few, to prove fusion imaging, actual, diagnostic accuracy. However they found two others important advantages, such as the possibility to detect a lesion in patients with reduced renal function and to reduce radiation exposure during follow-up.

Stang's group too, evaluated colo-rectal liver metastasis using fusion-imaging technique. They found a better characterization of small hepatic lesions, with a higher rate of correctly classified nodules compared with CT imaging alone.

Fusion imaging was tested also in breast biopsy. MR imaging in fact has an high sensitivity in the detection of breast cancer even if it shows a variable specificity. Above all, there is a large overlap of MRI features of the lesions, during the enhancing phase, which influences patient's management. Moreover MRI guidance for biopsy shows many disadvantages above all regarding cost and time. Many groups of research try to reach MR suspicious with a second look US examination, for all these reasons Rizzatto and Fausto tested the feasibility of fusion guidance in breast imaging.

An important problem is the different position of the patient during US examination and during MRI scan, such as the mobility of breast tissue. In fact usually breast is examined

using clock position. To solve this problem different approaches were proposed, such as the use of algorithms to develop a model of deformation or the use of a redesigned bed that allows to lie in the prone position both during US and MRI examination. In the first case the registration phase is made using target points that are identified between the two images, obtained with different modalities, and then transformed. After US-MRI imaging coregistration, the software reconstructs a real time multiplanar MR image of the corresponding US examination. Particularly Rizzatto and Fausto performed their first MRI examination in the prone position, using precontrast and postcontrast phases, then they obtained another MRI data set with the patient in the supine position by using external fiducial markers at 9-, 12- and 3- o'clock. So they performed US live examination with the patient in the supine position. Using fusion imaging guidance for breast biopsy, the authors reached an important reduction of the time and costs.

About pain therapy Galiano's group first conducted a research in 2007 that analyzed a kind of fusion imaging. Galiano's group tried to improve US visualization of facet vertebral joint to pain therapists unfamiliar to US scan, that however would like to perform medial branch block with US guidance. They used CT reconstruction images to recognize the anatomical structures during real time US examination of the facet joints. Their research was conducted only on cadavers with subsequent good results. In fact, at the end of the study, they encouraged to start to perform anesthetic blocks in real patients under an US guide.

Klauser and Zacchino's groups published the first papers analyzing fusion imaging in pain therapy in 2010.

Klauser tested fusion imaging to guide sacro-iliac joint-infiltration, using ten cadavers and then ten patients. The basic concept of fusion imaging is always the same, so also Klauser's group chose anatomical target points to match US with CT. Particularly the landmarks were spinous process of the fifth lumbar vertebra, posterior superior and inferior iliac spine, first and second posterior sacral foramen and the sacro-iliac joint. They found a positive success rate, with an increasing learning curve in the second half of patients. Moreover CT scan provides further anatomical details about joint assessment, about eventual bone spurs and so on.

In this work too, registration time takes the longest time, but is the most important time of the entire procedure.

Zacchino's group tested the feasibility of pudendal nerve anesthetic block using fusion imaging. In this work US was matched with CT data, using as anatomical target points ischiatic spine, femoral head and coccyx. They performed anesthetic block in the Alcock's canal, which is difficult to reach using an US or CT guidance alone. Fusion imaging provides further anatomical details for this block, such as the possibility to visualize with the same technique both the pudendal vascular bundle, sacrotuberous and sacrospinous ligaments, independently from pudendal nerve depth. After the procedure the patient was immediately and completely pain free.

All these works carried out on different interventional procedures showed that fusion imaging is helpful to reach the region of interest, and that fusion imaging, combining CT spatial resolution and its wide field of view, with US real time, is essential to perform the procedure, avoiding possible complications (unintended puncture of vessels, hematoma, etc). Fusion imaging improves direct visualization of the region of interest matching CT/MRI advantages plus US advantages avoiding radiation exposure during the procedure, that is always important but above all when repeat the procedure is mandatory and in young patients. It avoids also US disadvantages, first of all, its dependence on patient body

mass index. However using fusion imaging too, requires a certain experience that lead to decrease procedure time and it improves the success rate.

Moreover it's important to place the patient in the same position, both during the CT/MRI previous acquisition and during the procedure, as Crocetti proved. Then it's important also to avoid patient's movement both during registration time and during the procedure.

Fusion imaging technique however is now applied to others different kind pathology: a new report (Iagnocco 2011) evidences some possibilities in rheumatologic field, where fusion is used to investigate and monitor osteoarthritis and rheumatoid arthritis. This paper showed as fusion imaging should be useful for therapy monitoring matching MRI anatomical landmarks and US details.

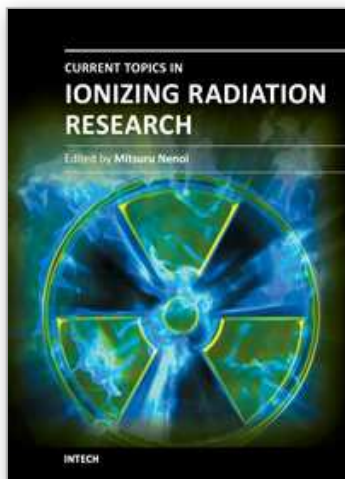
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Since the discovery of X rays by Roentgen in 1895, the ionizing radiation has been extensively utilized in a variety of medical and industrial applications. However people have shortly recognized its harmful aspects through inadvertent uses. Subsequently people experienced nuclear power plant accidents in Chernobyl and Fukushima, which taught us that the risk of ionizing radiation is closely and seriously involved in the modern society. In this circumstance, it becomes increasingly important that more scientists, engineers and students get familiar with ionizing radiation research regardless of the research field they are working. Based on this idea, the book "Current Topics in Ionizing Radiation Research" was designed to overview the recent achievements in ionizing radiation research including biological effects, medical uses and principles of radiation measurement.

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