35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Virtual Navigator Real-Time Ultrasound Fusion Imaging with Positron Emission Tomography for Liver Interventions

Enzo Di Mauro, Marco Solbiati, Stefano De Beni, Leonardo Forzoni, Sara D'Onofrio, Luigi Solbiati

Abstract— **Real-time fusion imaging technologies are increasingly being used among interventional radiologists, mostly Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) dataset, fused with Ultrasound (US) imaging. In addition, fusion of Positron Emission Tomography (PET) and CT is increasingly diffused in clinical practice, due to the wide availability of PET scanners and the capability to make either a direct (acquisitions performed within the same system) or an indirect (procedure performed on an external workstation, merging the two different sets of acquired data) fusion with CT data. The present work describes the feasibility of real-time fusion imaging directly between PET data and US imaging, with CT scans being used only for PET-US fusion registration. Data on multimodality registration precision and clinical applications are presented as well.**

I. INTRODUCTION

In recent years real-time Ultrasound (US) image fusion with a pre-acquired second imaging dataset - Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI) [1] - has become widely used in both diagnosis and image-guided interventions, being liver and kidneys the main anatomical districts of clinical application [2-9]. Additionally, PET-CT fusion imaging is being increasingly used in clinical practice, due to the wide availability of Positron Emission Tomography (PET) scanners and the capability to make either a direct (acquisitions performed within the same system) or an indirect (procedure performed on an external workstation, merging the two different sets of acquired data) fusion with CT data. The present work describes the feasibility of real-time fusion imaging directly between PET data and US imaging, with CT scans being used only for PET-US fusion registration. The possibility to have real-time functional information from the examined tissues achieved with PET [10], while performing US-guided and/or CEUS (Contrast-Enhanced US)-guided [11] interventional procedures, represents a valuable additional tool. US is the most widely diffused imaging modality for guidance and monitoring of both diagnostic (biopsy, fine-needle aspiration, etc..) and therapeutic (drainage of fluid collection, ethanol injection, thermal ablation, etc..) interventional procedures in organs visible with US. This is due to its sensitivity for the detection of small targets (particularly if coupled with injection of contrast agents), nearly universal availability, portability, ease of use and low cost, but mostly to its real-time capability (US) that allows to follow the interventional procedure in all its phases [12-14]. However, US has also some limitations, like patient's body habitus, bowel gas distention, insufficient sensitivity for the detection of small lesions in some conditions (obesity, underlying diffuse parenchymal disease, history of previous treatments affecting organ structure, etc.). When the target lesion is not or poorly visualized by US and well depicted by CT or MRI, real-time US-CT/MRI fusion imaging can significantly help its detection and the subsequent interventional procedure [15-17]. However, in some clinical occurrences, target lesions are better or even exclusively visualized by PET-CT, thanks to the functional information that this modality provides. Therefore the need for fusing real-time US with PET-CT before starting the interventional procedure can be strongly felt.

The present work is a preliminary study on the feasibility and practical execution of direct PET-CT/US real-time fusion imaging for abdominal interventions. Data obtained by tests performed on a multimodality phantom, for the assessment of the precision of the registration procedure and in-vivo interventional procedures, are presented.

II. MATERIALS AND METHODS

A. Study population

Five patients (2 males and 3 females, age range: 51-80 yrs, mean: 67.8) with a history of resection of colon carcinoma underwent follow-up PET, CT and US examinations after signing a written informed consent. In three patients a single hepatic metastasis was found, in the remaining two, that previously underwent percutaneous thermal ablation for multiple hepatic metastases, local progression of one the metastases ablated was detected. All the lesions (size range: 1.3 – 2.7 cm, mean: 1.8) were not visible on US and contrast-enhanced CT, but only detected by PET. All the patients were not surgical candidates and therefore they were scheduled for percutaneous thermal ablation.

B. Methods of examination

24 hours before the scheduled thermal ablation treatment, each patient underwent PET-CT scan. CT acquisition was obtained first and subsequently PET was performed. PET and CT examinations were carried out by a Biograph 6 True Point (Siemens Medical Solutions, Knoxville, TN, USA) PET-CT scanner. CT acquisition parameters: tube voltage 130kV, tube current 206mA, 120mAs, coll 2, slice 3, pitch

E. Di Mauro is with Dept. of Nuclear Medicine, General Hospital of Busto Arsizio (VA), Italy.

M. Solbiati is with Faculty of Biomedical Engineering, Polytechnic, Milan, Italy.

S. De Beni, L. Forzoni (corresponding author. Phone: +39 055 4229427; fax: +39 055 4229422; e-mail: leonardo.forzoni@esaote.com) and S. D'Onofrio, are with Esaote S.p.A., Genova, Italy.

L. Solbiati is with Dept. of Interventional Oncologic Radiology, General Hospital of Busto Arsizio (VA), Italy.

factor (volume pitch) 1.65; PET examination was with 2min/acquisition. The global CT-PET acquisition time was 20 minutes. The CT field of view (FOV) covered properly the entire volume of the liver and the adjacent organs and structures. CT in portal phase, used for the reconstruction of the volume necessary for the US fusion, was performed on liver parenchyma only. 18F-FDG (Fluorodeoxyglucose) radioactive tracer was intravenously administered 1 hour before PET acquisition at the dosage of 4 MBq/Kg. 18F-FDG is a molecule analogous to glucose, with an hydroxide replaced by fluorine 18 (nuclide) [10]. Cells with increased glucose metabolism, like most neoplastic cells, have a much greater uptake of 18F-FDG than normal cells. Accordingly, this tracer is extensively used for the detection of neoplastic tissue [10, 18]. Subsequently, real-time image fusion of US and pre-acquired PET-CT data was performed using an US system (MyLab Twice, Esaote S.p.A. Italy) equipped with Virtual Navigator (VN) option [19]. PET-CT data were transferred in DICOM format to the US system through a LAN connection, query/retrieving hospital PACS system (IMPAX 6, Agfa Healthcare NV, Mortsel, Belgium). A US convex Array Probe (Operating Bandwidth: 1- 8 MHz; CFM-PW Frequencies: 1.9 - 2.1 - 2.3 – 2.6 – 3.3 MHz, CA541, Esaote) and a reusable tracking bracket with sensor mounted (639-041, Civco Medical Solutions, Kalona, Iowa, USA), were used. The appleprobe design of this probe allowed a dual-possibility hand grip, pinch and palmar grip, in order to provide a neutral wrist position [20]. This represented an operator's additional comfort, considering that the whole treatment procedure could have had a long duration, especially during the treatment phases of planning, execution and monitoring.

C. Registration Procedures: PET-CT and CT-US

Fusion imaging between CT and PET data was obtained with a registration performed automatically by the PET-CT dedicated workstation. The multimodality registration precision declared by the system producer is 1 mm (Fig. 1).

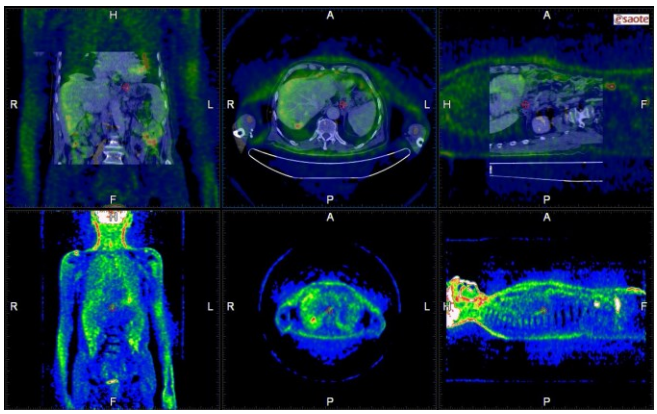
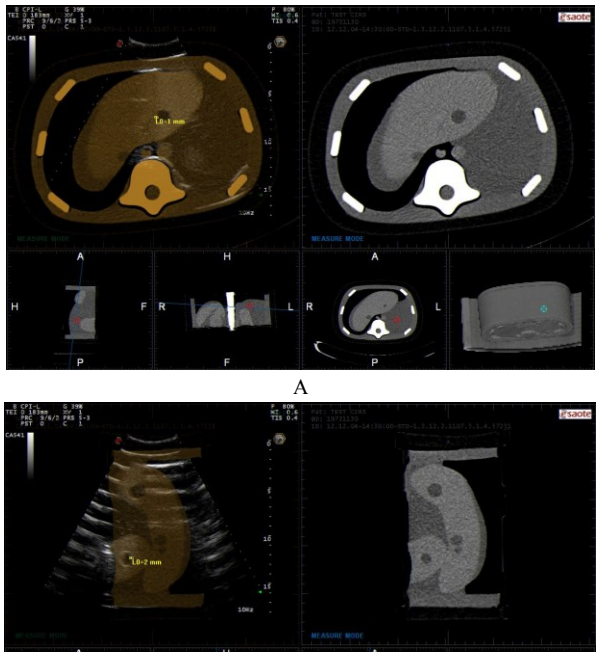


Fig. 1. Image data fusion between PET and CT acquisitions

Fusion imaging between CT and US was initially carried out and tested for precision through dedicated in vitro tests, performed with a commercially available triple modality 3D abdominal phantom (Model 057, CIRS - Computerized Imaging Reference Systems Inc., Norfolk, Virginia, USA). The phantom CT scan was performed by a HiSpeed CT (GE Medical Systems, Milwaukee, Wisconsin, U.S.A.), slice thickness = 5 mm (2.0x2.0 mm in-plane resolution). This CT evaluation can be considered equivalent to the one used for the in vivo tests, for the purposes of this work. Virtual Navigator fusion procedures were allowed by an electromagnetic tracking system, composed by a transmitter and a small receiver, mounted on the US probe. The transmitter's position, which is the origin of the reference system, was fixed by a support and the receiver provided the position and the orientation of the US probe in relation to the transmitter in the created 3D space. The electromagnetic field source tip was oriented to point to the phantom, in order to address the highest intensity of the created field to the US scanning area. A non-metallic table was used to reduce interferences as much as possible. Before starting, a check of the accuracy of the electromagnetic field was performed: the same point coordinates were measured twice by a proper registration pen with the electromagnetic sensor mounted in two different spatial orientations. An accuracy of 0.2 cm or less was considered acceptable. After importing the CT phantom data on the US system in DICOM format by DVD support, the system was ready to start the fusion procedure between CT and real-time US data, applying anatomical-like registration with internal markers (kidney-like, vessel-like and lesion-like). The procedure was considered successful if the root mean square error between the anatomical markers settled on US and the set points on the CT volume dataset loaded on the US system was 0.5 cm or less. After the procedure, moving the US probe, real-time US scans of the phantom and simultaneous navigation within its CT volume were achieved. A further improvement of registration was achieved, performing a fine-tuning adjustment referring to anatomical points different from the previous ones. At the end, visual control of the correspondence of anatomical structures on US and CT in axial, coronal and sagittal views during navigation and measurements of the size of liver-like and kidney-like lesions contained in the phantom (Fig. 2) were used as assessment of the accuracy of the registration procedure.



A

B

Fig. 2. Axial view (A) and sagittal view (B), probe perpendicular to the phantom echogenic side, measurement of liver-like lesions taken.

The in vivo registration procedure for fusion of CT and US dataset was carried out similarly. After checking the accuracy of the VN electromagnetic field, registration with hepatic anatomical markers (vascular tree) was carried out and liver morphology (through subsequent fine-tuning adjustments) was used as tool for the assessment of precision, considering a discrepancy of 0.5 cm. as satisfactory. Subsequently, PET data were retrieved without performing an additional registration procedure, obtaining an "indirect" real-time image fusion of US and PET (Fig. 3).

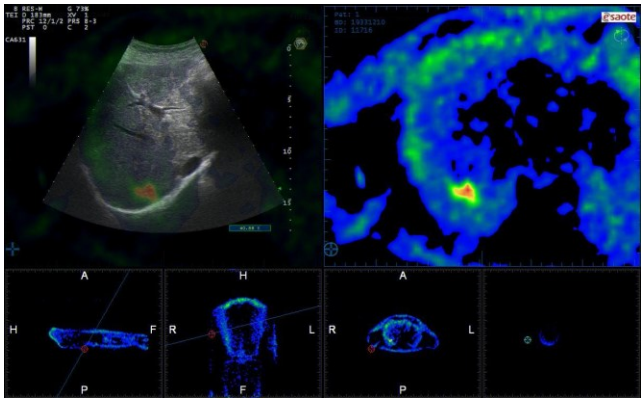
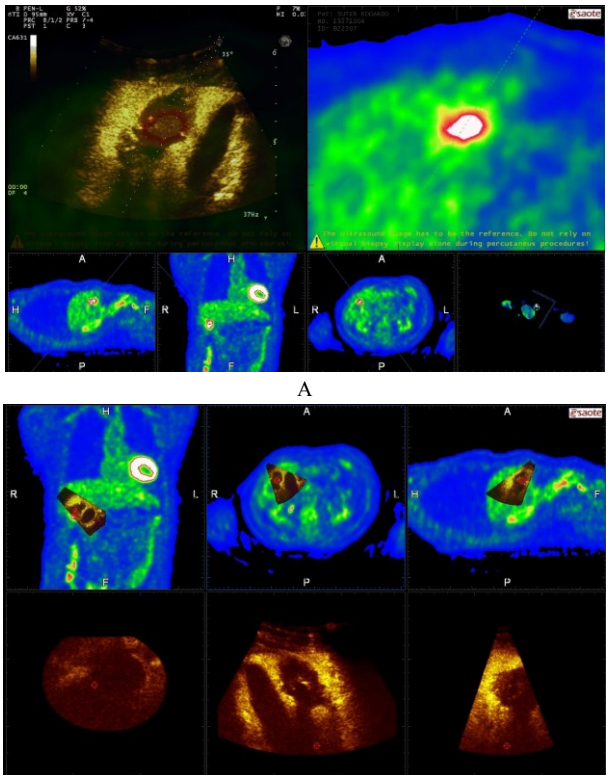


Fig. 3. PET – US real-time fusion

D.Interventional Procedure

After the registration, the ablation procedure, guided by US, started with the selection of the thermal device. All the treatments were performed with a 14G, internally cooled microwave needle-like antenna connected to a high-power generator (AMICA, HS Hospital Service S.p.A., Pomezia, Italy). Pre-procedural planning (number of antenna insertions needed and other settings) was performed on the US system, with the graphic representation, provided by the VN tool, of the expected volume of necrosis, achievable with the selected type of antenna, overimposed on PET data. The US visualization of needle path was provided by the use of biopsy brackets coupled with needle guide (Ultra-Pro III, CIVCO Medical Solutions, Kalona, Iowa, USA). In order to virtually visualize needle path and needle tip also on the second imaging modality, a reusable, non-sterile, general purpose sensor (VirtuTrax, CIVCO Medical Solutions, Kalona, Iowa, USA) attached to a sterile disposable item and secured to the MW antenna was used as a second electromagnetic sensor. This was very helpful to select the best path to reach the target, the percutaneous access point and the antenna angulation; moreover to track the needle tip position also during ablation, when gas developed by heating completely blocked target visibility on the US [8]. After ablation, CEUS with second-generation contrast agent (SonoVue, Bracco, Milano, Italy) was performed, in order to assess the immediate result of the treatment: the volume of necrosis achieved with 3D CEUS was compared (and overlapped) with the one of the pre-treatment lesion showed by PET (Fig. 4).



A

B

Fig. 4. CEUS after ablation treatment, fused with pre-acquired PET. A) real-time CEUS-PET fusion imaging; B) CEUS-PET volume dataset fusion.

III. RESULTS

Six tests to assess the registration precision of CT and US datasets were performed on the multimodality abdominal phantom. Three tests were performed by placing the phantom at a fixed distance (38 cm) from the VN transmitter (distance measured from the center of the electromagnetic transmitter to the center of the phantom), repeating the registration phase each time and measuring the axial, coronal and sagittal views of three points for each registration. Results are shown in Table 1.

TABLE I. VIRTUAL NAVIGATOR PRECISION REPEATING REGISTRATION, SAME PLACE

Acquisition	Measured point	Registration error axial plane (mm)	Registration error coronal plane (mm)	Registration error sagittal plane (mm)
1	A	2	2	2
1	B	2	2	2
1	C	2	2	2
2	A	3	1	2
2	B	1	3	2
2	C	0	2	3
3	A	2	1	1
3	B	2	1	3
3	C	1	2	2

Three tests were then performed by placing the phantom at different distances from the transmitter (23, 38 and 40 cm), repeating the registration phase after each distance change and measuring the axial, coronal and sagittal views of one point for each registration. Results are shown in Table 2.

TABLE II. VIRTUAL NAVIGATOR PRECISION REPEATING REGISTRATION, CHANGED POSITION IN SPACE

Acquisition	Measured point	Registration error axial plane (mm)	Registration error coronal plane (mm)	Registration error sagittal plane (mm)
23 cm distance	A	1	1	2
38 cm distance	A	2	2	2
40 cm distance	A	3	2	1

The average registration error measured on the phantom is directly proportional to the distance from the electromagnetic transmitter, remaining in the field limits where the magnetic field produced by the tracking system is greater than the Earth's magnetic field. This limit is at 78 cm (30.7 inches) from the transmitter. The maximum registration error related to different registrations was 3 mm. This value can be reasonably considered the minimum registration error which can be obtained during in vivo CT-US fusion imaging procedures. In the clinical cases, the respiratory activity had a significant impact on the registration error, as previously reported in literature [16, 22]. Regarding PET-US fusion, when in vivo co-registered PET-CT with US was obtained and then only PET data fused with US were considered, a minimum average global registration error of 3 mm was measured, as probably due to the PET-CT registration error.

All the ablative treatments were successful, without any complication. The amount of energy to be administered was calculated for each lesion, aiming at a minimum "safety margin" of 5-7 mm beyond the lesion margins showed by PET, considering also the possible errors caused by respiratory movement and the PET-CT and CT-US registration errors.

IV. DISCUSSION AND CONCLUSION

Virtual Navigator fusion imaging system allows to visualize US scans co-registered in real-time with other reference imaging modalities (CT, MRI, PET, 3D-US) [2, 22], overlapped or visualized side by side. Real-time PET-US fusion must use CT data as an intermediate means of co-registering. This preliminary study demonstrated that real-time fusion of US and PET modalities by Virtual Navigator tool can improve the anatomical localization of actively uptaking lesions and this is extremely important in cases of poor or absent visualization of lesions on US alone, as it was reported in a recent paper [23]. Moreover, Virtual Navigator enabled easier differentiation between uptaking and non-uptaking lesions on PET. CEUS after treatment and its direct fusion with pre-treatment PET ensured a higher level of confidence also in the follow-up phase.

In conclusion, real-time PET-US fusion allowed treatments that otherwise, basing on PET-CT alone, with no real-time capabilities, would have been technically difficult. Fusion with PET made US a real-time functional modality.

REFERENCES

[1] L. Zhou et al., "A robust registration method for real-time ultrasound image fusion with pre-acquired 3D dataset", *Conf Proc IEEE Eng Med Biol Soc.* 2011:2638-41.

[2] Crocetti L, Lencioni R, De Beni S et al, "Targeting liver lesions for radiofrequency ablation: an experimental feasibility study using a CT-US fusion imaging system", *Invest Radiol* 2008; 43: 33-9.

[3] Krücker J, Xu S, Venkatesan A et al, "Clinical utility of real- time fusion guidance for biopsy and ablation". *J Vasc Interv Radiol* 2011; 22(4):515-24.

[4] Milot M, Ma K, Efford E, et al, "Evaluation of a multimodality MR/US coregistration system for investigation of hepatic metastases from colorectal cancer", *J Vasc Interv Radiol* 2013 (in press)

[5] Minami Y, Chung H, Kudo M "Radiofrequency Ablation of Hepatocellular Carcinoma: Value of Virtual CT Sonography with Magnetic Navigation", *AJR Am J Roentgenol* 2008; 190(6): 335-41.

[6] Sandulescu DL, Dumitrescu D, Rogoveanu I, Saftoiu A, "Hybrid ultrasound imaging techniques (fusion imaging)", *World J Gastroenterol* 2011; 17(1):49-52.

[7] Wood BJ, Kruecker J, Abi-Jaoudeh N et al, "Navigation systems for ablation", *J Vasc Interv Radiol* 2010; 21(8 Suppl): S257–S263.

[8] Wood BJ, Locklin JK, Viswanathan A et al, "Technologies for guidance of radiofrequency ablation in the multimodality interventional suite of the future", *J Vasc Interv Radiol* 2007; 18(1): 9-24.

[9] Wood BJ, Zhang H, Durrani A et al, "Navigation with electromagnetic tracking for interventional radiology procedures: a feasibility study", *J Vasc Interv Radiol* 2005; 16(4): 493-505.

[10] Mian M Alauddin, "Positron emission tomography (PET) imaging with 18F-based radiotracers", *Am J Nucl Med Mol Imaging* 2012; 2(1): 55-76.

[11] Solbiati L, Ierace T, Tonolini M, Cova L, "Guidance and monitoring of radiofrequency liver tumor ablation with contrast-enhanced ultrasound", *Eur J Radiol* 2004; 51 Suppl: S19-23.

[12] Holm HH, Skjoldbye B, "Interventional ultrasound", *Ultrasound Med Biol* 1996; 22: 773-89.

[13] Otto R, "Interventional ultrasound", *Eur Radiol* 2002; 12: 283-87

[14] Machi J, Uchida S, Sumida K et al, "Ultrasound-guided radiofrequency thermal ablation of liver tumors: percutaneous, laparoscopic, and open surgical approaches", *J Gastrointest Surg* 2001; 5(5): 477-89.

[15] Kawasoe H, Eguchi Y, Mizuta T et al, "Radiofrequency ablation with real-time virtual sonography system for treating hepatocellular carcinoma difficult to detect by ultrasonography", *J Clin Biochem Nutr* 2007; 40(1): 66-72.

[16] Liu FY, Yu XL, Liang P et al, "Microwave ablation assisted by a real-time virtual navigation system for hepatocellular carcinoma undetectable by conventional ultrasonography", *Eur J Radiol* 2012; 81(7): 1455-59.

[17] Nakai M, Sato M et al, "Radiofrequency Ablation Assisted by Real-Time Virtual Sonography and CT for Hepatocellular Carcinoma Undetectable by Conventional Sonography", *Cardiovasc Intervent Radiol* 2009; 32: 62–69.

[18] Sacks A, Peller PJ, Surasi DS, et al, "Value of PET/CT in the management of liver metastases, part 1", *AJR Am J Roentgenol* 2011; 197(2): 256-9.

[19] De Beni S, Macciò M, Bertora F, "Multimodality Navigation Tool 'Navigator'", in *Proc. IEEE SICE 2nd International Symposium on Measurement, Analysis and Modeling of Human Functions*, Genova, Italy, 2004.

[20] Forzoni L et al., "Case Study of Integrated Ergonomic Assessment of a Portable Ultrasound System", in *Advances in Human Aspects of Healthcare* (ISBN 9781439870211), CRC Press, 2012.

[21] Forzoni L et al., "Virtual Navigator Tridimensional Panoramic Imaging in Transcranial Application", Biomed Tech 2012; 57: 38–41

[22] F.L. Giesel, "Image Fusion using CT, MRI and PET for treatment planning, navigation and follow up in percutaneous", *Exp Oncol.* 2009; 31(2): 106–14.

[23] Venkatesan AM, Kadoury S, Abi Jaoudeh N et al, "Real-time FDG PET Guidance during Biopsies and Radiofrequency Ablation Using Multimodality Fusion with Electromagnetic Navigation", *Radiology* 2011; 260(3): 848-56.