Multi-parametric Image Fusion for Navigation and Follow up in Radiofrequency Tumor Ablation

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Introduction

Image Fusion (co-registration) is by no means a new post processing technique [1]. There are numerous technical approaches described to combine imaging data obtained from different modalities [2]. Algorithms for co-registration of functional and anatomical data sets has been shown in fixed organs such as the brain [3,4] but also in organs subject to respiratory motion, such as the lung [5]. Major challenges due to motion and the non-rigid nature of abdominal organs (such as the kidney and the liver) have limited the use image fusion. Co-registration has proven useful in the evaluation of patients with cancer for diagnostic / staging and monitoring the response to therapy [6]. Minimal invasive image-guided therapy like radiofrequency thermal ablation (RFA) has become very popular recently, especially in the liver, lung, bone and kidney, [7] and may improve survival for certain patients [8].

Optimal outcomes of percutaneous RFA are however dependent upon accurate targeting of the neoplastic tissue and monitoring of the resulting thermal lesion. Success of treatment is intimately linked to the volumetric spatial relationship of neoplastic tissue to the thermal lesion margins. An accurate understanding of this relationship that is readily accessible may provide feedback during pre-treatment planning, procedural navigation, and early detection of re-growth. Image guidance for RFA necessitates accurate probe placement to effect sphere-packing with sufficient overlap to avoid gaps of sub-lethal heating, and to include a small margin of normal tissue ("safety margin") beyond the neoplastic tissue borders. This can be a challenging task prone to human error. Image fusion was therefore used as a post-processing tool to help oncologic treatment planning and to guide the interventional radiologist before, during, and after the RFA procedure.

Purpose

To determine if image fusion of morphological and functional image data can facilitate treatment planning, probe placement, probe re-positioning, and early detection of residual disease following radiofrequency ablation (RFA) of liver, kidney, and adrenal tumors. To perform image fusion retrospectively to help visualize the relationship between thermal lesion margin and tumor margin. To detect residual tumors and to predict recurrence earlier, and to facilitate early repeat treatment before neoplasms become geometrically unfavorable for retreatment.

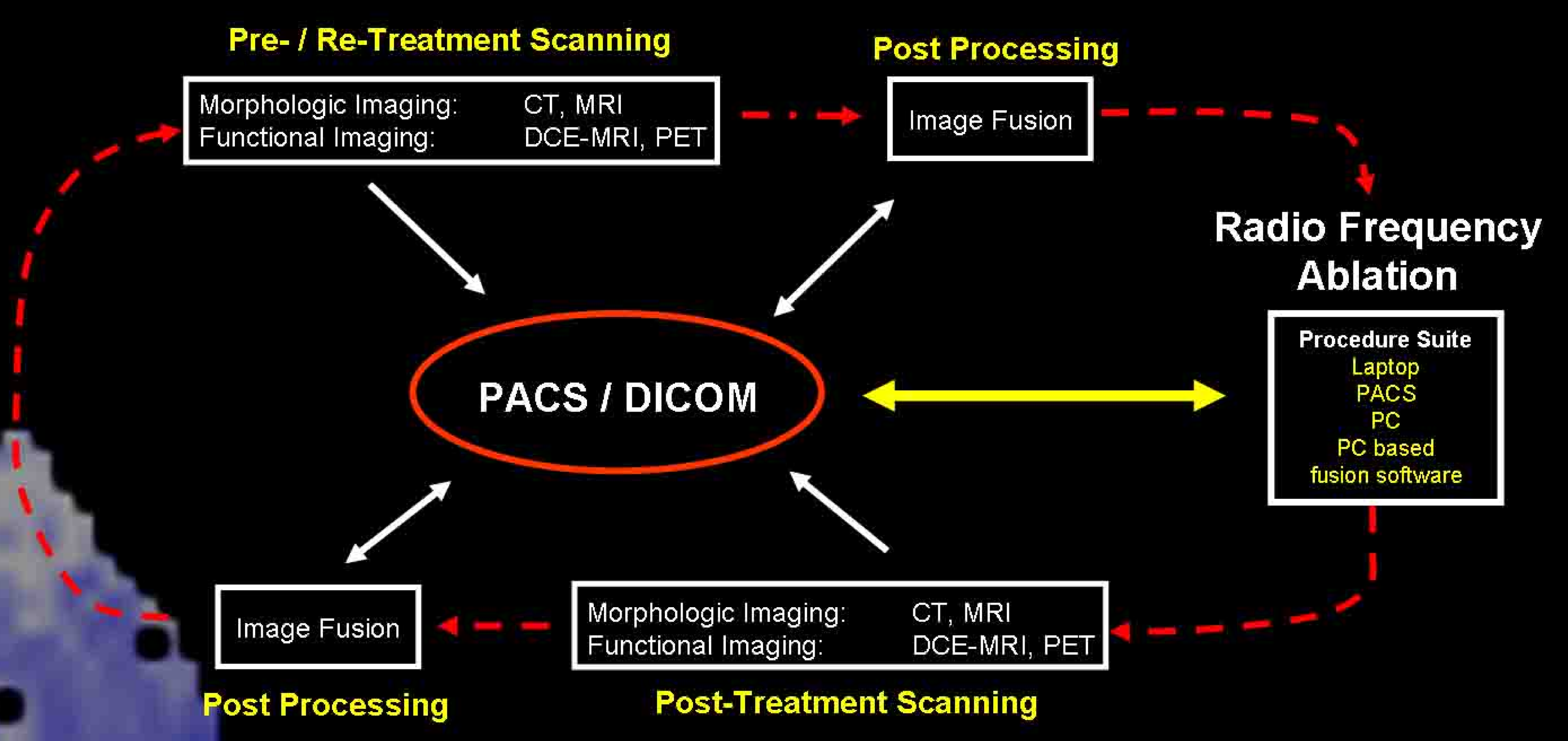


Fig. 1: Workflow diagram of the imaging data during treatment planning for RFA patients. After initial or follow up scanning DICOM images are co-registered using PC-based software. These images are transmitted to a laptop or to the PACS to be viewed during the RFA procedure. Post treatment re-evaluation imaging is conducted with the same modalities and same protocol. Results of Image Fusion of pre and post treatment image data sets are used for therapy assessment.

Method and Material

Patients

Image fusion was performed on 33 tumors in 20 patients undergoing RFA for the treatment of either liver or kidney tumors. Most post-treatment images used were taken approximately two months after the ablation was performed. Post-procedure imaging was also fused to pre-treatment imaging. Positron emission tomography (PET) was fused to computed tomography (CT) and magnetic resonance imaging (MRI), CT to CT, MR to MR, and CT to dynamic contrast enhanced (DCE)-MRI. Arrival of the contrast agent was timed to maximize the lesion margin conspicuity.

Imaging

Non-invasive evaluation of anatomic details (localization and definition of lesion morphology) was performed by acquiring CT (GE) or MRI (1.5T, GE) datasets. Nuclear medicine (FDG-PET, GE) and DCE-MRI were used to provide physiologic and functional (metabolic and biochemical) information. Image fusion (Fig. 2) was done between same (Fig. 3) as well as different modalities (Fig. 4).

Multi - Modality Image Co-Registration

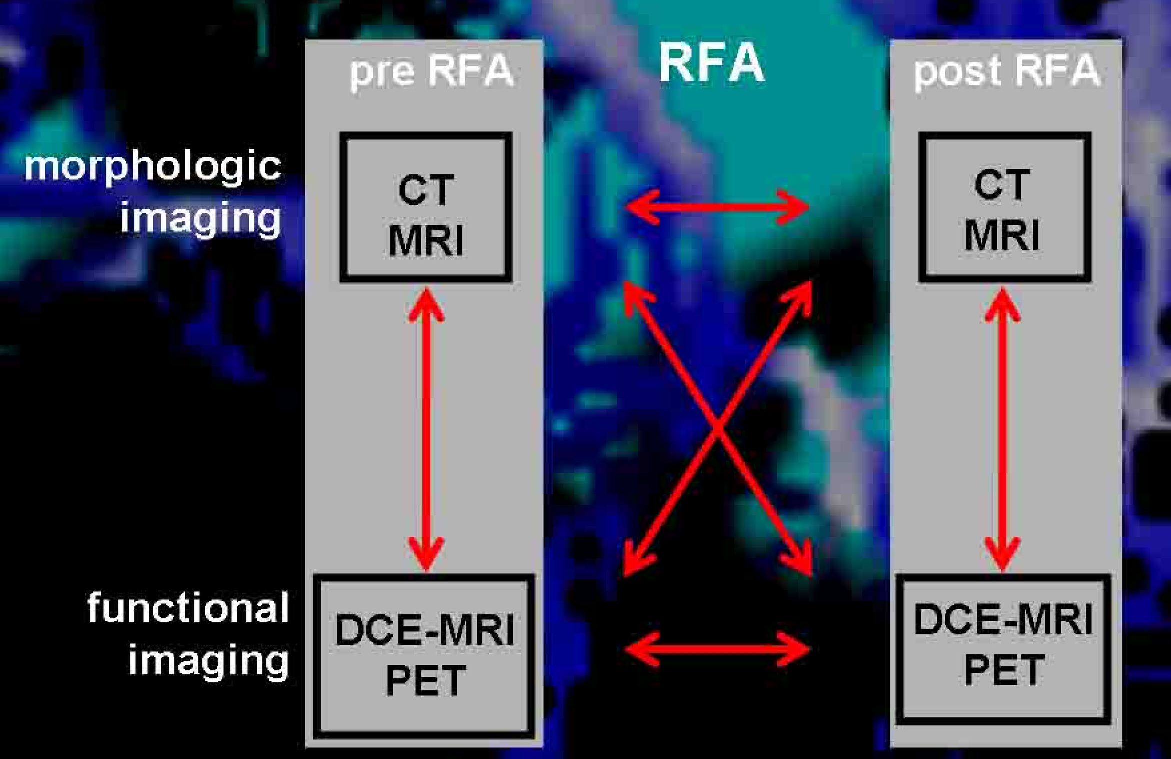


Fig. 2: Fusion can visualize tumors and thermal lesions prior to (orange box) and post (blue box) radiofrequency ablation. A number of fusion combi-nations are possible.

Intra - Modality Image Fusion (CT to CT)

Fig. 3: Image fusion (affine - 12 degrees of freedom) of pre and post CT studies. An affine registration model is typically sufficient to register these images. However, if artifacts (e.g. breathing) are significant, a non-linear model might be required to accurately register the datasets.

Inter - Modality Image Fusion (CT to PET)

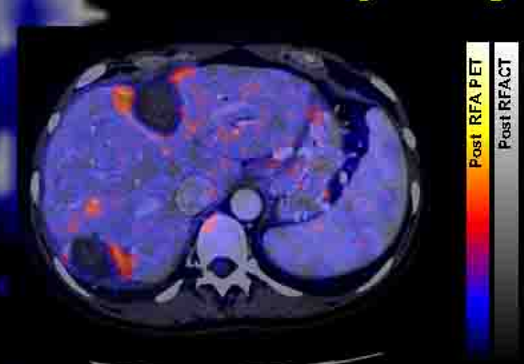


Fig. 4: Image co-registration of PET and CT datasets using a voxel simularity-based registration measure termed normalized mutual information (NMI) [13].

Post-processing

A NIH-written java-based software package (MIPAV, Medical Image Processing Analysis and Visualization, NIH) was used for image fusion [9]. The images were retrieved from the PACS (KODAK), registered, and visualized. Several methods of volume registration were examined: Least Squares Method [10], Thin-Plate Spline [11], and Optimized Automated Registration [12].

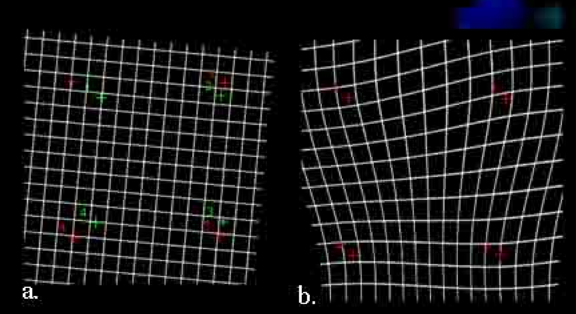


Figure 5: MIPAV image fusions. (a) Least squares is a rigid linear registration (rotation and translation) to find the least squared fit between two point sets (red and green points). (b) Thin-plate spline is a non-linear registration to register two images using point sets. Both of these techniques are easily extended into 3D.

Optimized Automated Registration (OAR)

Automatic Alignment using Rotation, Translation, Scale and Skew:
Twelve Degrees of Freedom

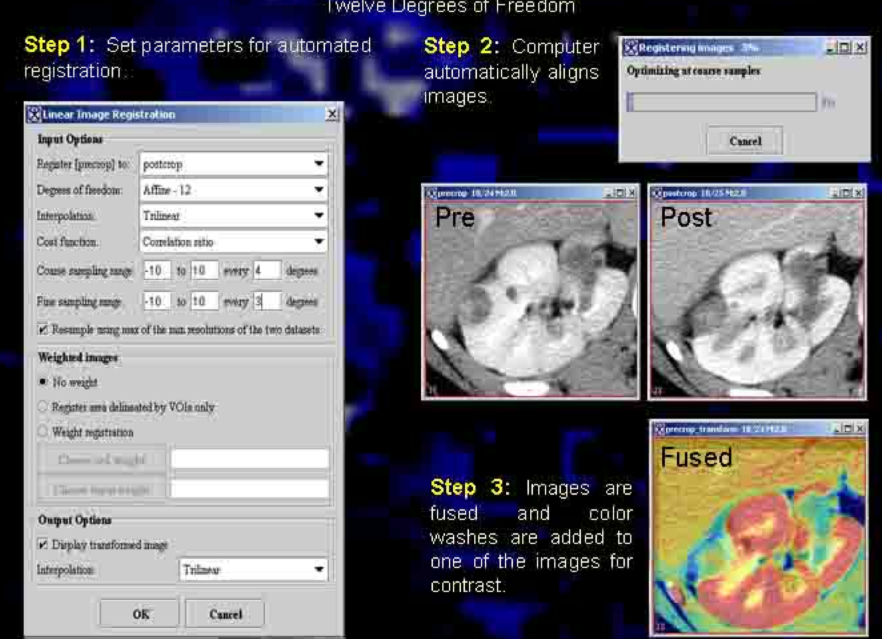


Fig. 6: Explanation of optimized automated registration, showing the actual parameters used for registration.

The least squares method of co-registration is a rigid transformation fusion. It uses anatomically similar landmarks, chosen by the user, in the two images that are to be fused, as shown in Figure 6. Using rotation and translation, which allows for six degrees of freedom, the least squares method minimizes the distance between the two sets of anatomic landmarks to register the two images (see example in Figure 5). Thin-plate spline is an alternate method that is non-linear and deforms or warps the images (see Figure 5) in an elastic fashion to fuse the anatomic landmarks chosen; an example of this method is shown in Figure 5. MIPAV also has the capacity to automatically register images using voxel simularity-based measures (i.e. mutual information, correlation ratios, cross correlation, etc.) using the optimized automated registration (OAR) method [12], as explained in Figure 6. This approach allows up to twelve degrees of freedom (3 rotations, 3 translations, 3 scales and 3 skews), and ultimately automatically fuses the images.

Therapy

Percutaneous image-guided radiofrequency ablation is a minimally-invasive technique to destroy neoplastic tissue. This procedure involves transforming a patient into an electric circuit. Grounding pads are placed on the patient's thighs. A small gauge, needle-like electrode (see Figure 7) that projects low frequency radio wave current is inserted into the patient's tumor using ultrasound (US) and computed tomography (CT) guidance. This alternating current causes oscillations among ions, or frictional energy, which increases the temperature to levels high enough to be lethal to all tissue surrounding the electrode.

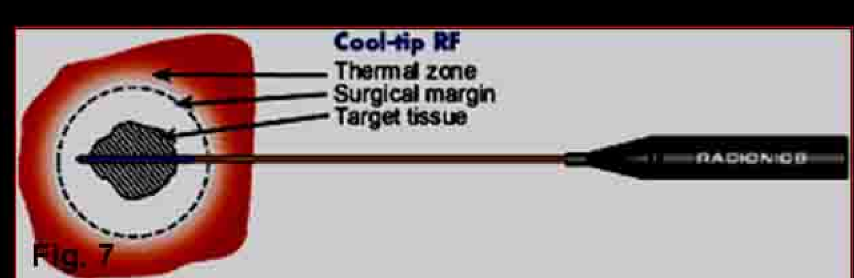


Fig. 7-8: Two common techniques for RFA are: Water-cooled or de-ployable electrodes.

Instantaneous cell death, or coagulation necrosis, occurs at temperatures ranging from 60-100º C; however, cell death also occurs at lower temperatures if the tissue is subjected to such lower temperatures for longer periods of time. Eventually, the necrotic tissue is replaced with fibrotic or scar tissue. Thus, the goal of this local treatment is to coagulate all of the local neoplastic tissue, while sparing as much normal tissue as possible. Insufficient heating of even a small portion of tumor results in residual disease and recurrent growth. Early detection of incomplete treatment provides the best chance for re-treatment before growth renders the disease geometrically unfavorable.

Results

Image fusion was possible in all studies attempted, with fusions of varying quality dependent upon organ shift, respiratory variation, lesion or organ shrinkage, and positional changes. In two of tumor fusions attempted, fusion was extremely suboptimal mostly likely due to significant organ shift and respiratory variation. The semi-manual methods (least squares, thin-plate splines) are typically time consuming for clinical routine navigation, whereas with the OAR technique, reasonable processing time could be achieved, allowing real-time fusion during treatments. Region cropping facilitated rapid processing. The semi-automated OAR technique proved to be the fastest and most reliable method for real-time navigation during treatments, but the other methods of rigid and elastic fusion were better in selected cases for specific patients.

Pre Treatment Planning (initial / re-evaluation)

Fusion Images provide more exact targeting information as presented in Fig. 9,12,13; not all lesions are metabolically active. Fusion facilitates treatment planning and selection of appropriate therapy. Fusion of different sequences can take advantage of the strength of each sequence (to optimize anatomy and pathology).

During Intervention

Image fusion may facilitate needle placement (Fig. 10,12,13). Fusion of pre treatment imaging can direct needle placement and define targets. Online fusion during procedures may confirm margins. Fusion of pre treatment tumor and immediate post treatment thermal lesion defines margins when the information is most helpful.

Fusion of Morphology (MRI) and Function (PET)

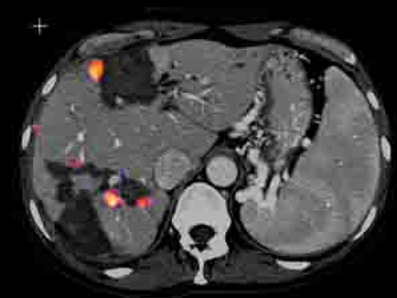


Fig. 9: After one RFA session fused images diagnose residual tumor, which can than be ablated again.

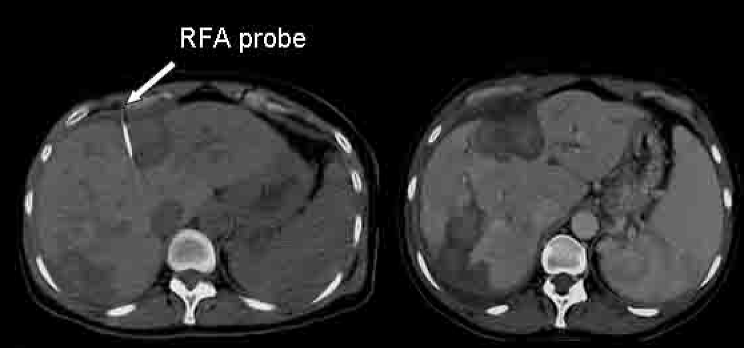


Fig. 10: Needle placement based upon fused images.

Fig. 11: Successful RFA retreatment.

PET and CT Fusion Validates Margin

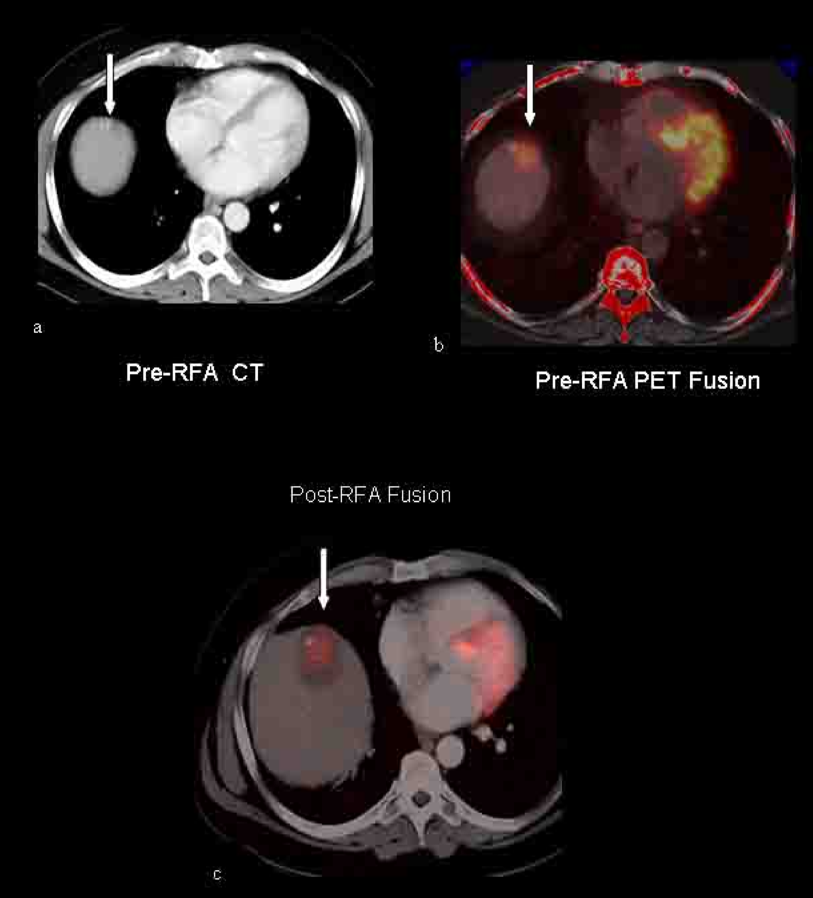


Fig. 12a-c: Mental co-registration could result in targeting error. Tumor is adjacent to white calcified scar (a). Fusion shows tumor is adjacent to white calcification (b). Post RFA fusion verifies RFA margin (c).

Image Fusion Detects Residual First

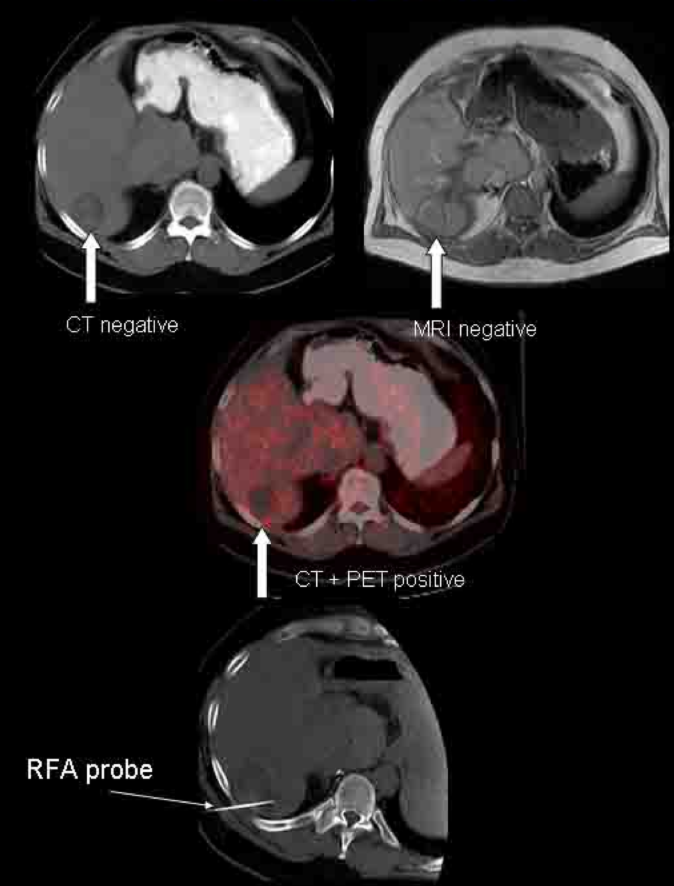


Fig. 13: CT and MRI post initial RFA were negative. PET and CT – PET fusion diagnosed residual tumor along posterior border first.

Post Treatment Assessment

Retrospective analysis may be performed to identify residual or recurrent tumor at the earliest possible time. Early detection may facilitate re-treatment before re-growth become geometrically un-manageable. Fusion of a 3D surface display gives a spatial representation of tumor and its relation to the thermal lesion (Fig. 17).

Multi - Modality Co-Registration

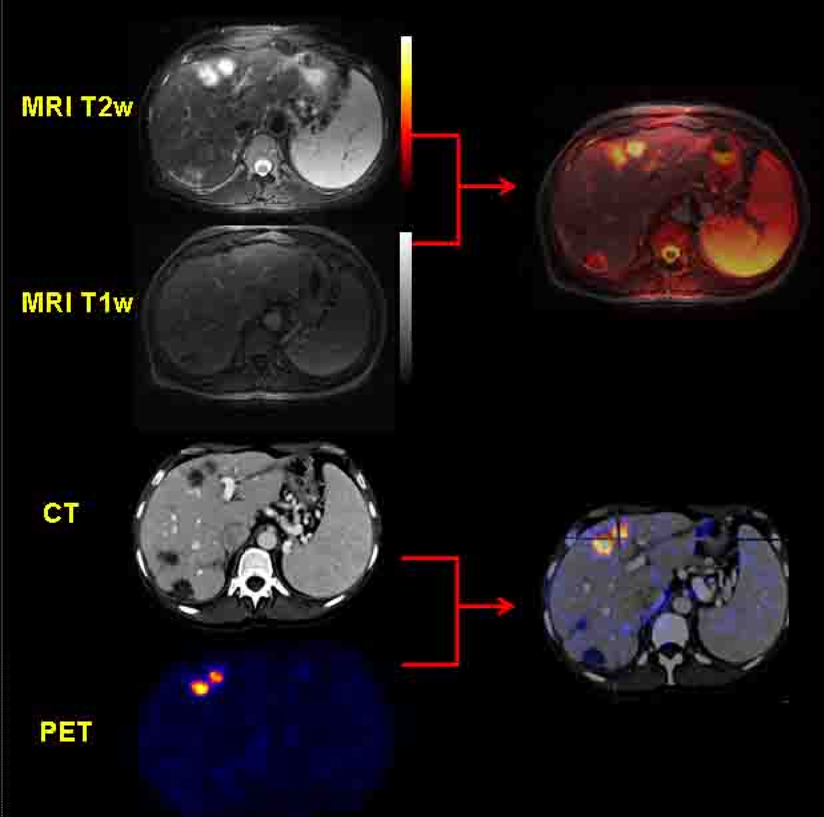
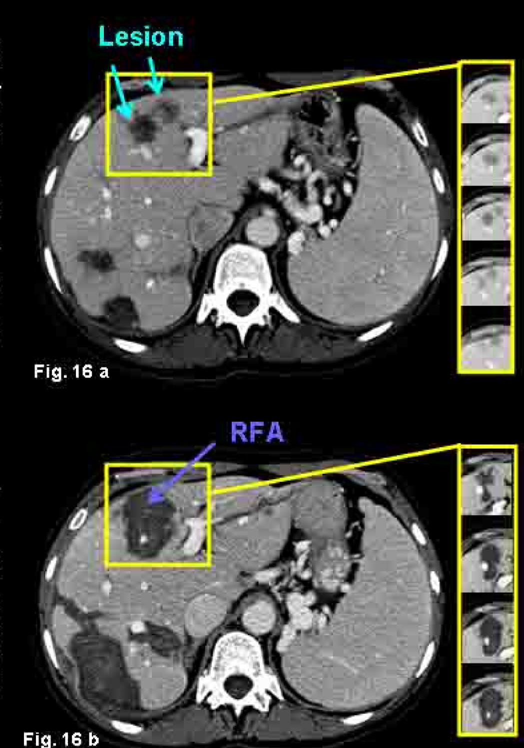
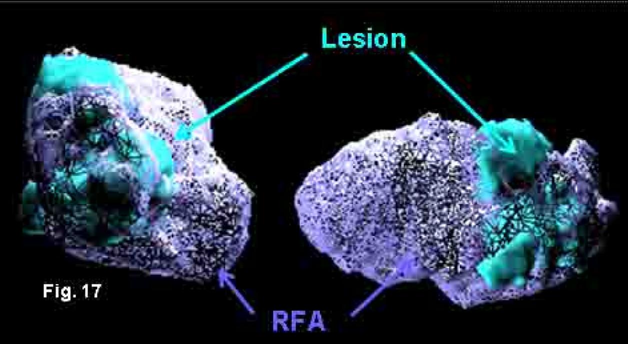


Fig. 14: T1w and T2w MR images before and after fusion of the two data sets. To improve fusion, the T2w images are visualized within a color-palette whereas the T1w images kept within a grey scale.

Fig. 15: CT and FDG-PET Inter-Modality Co-Registration to clarify morphology by differentiating scar and tumor. Scar (posterior) and tumor (anterior).





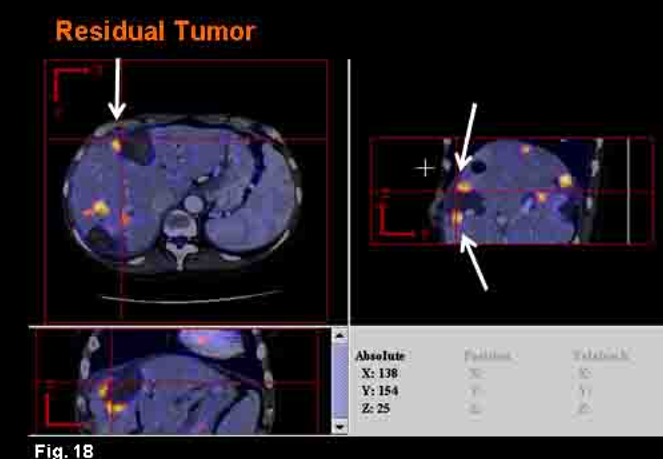
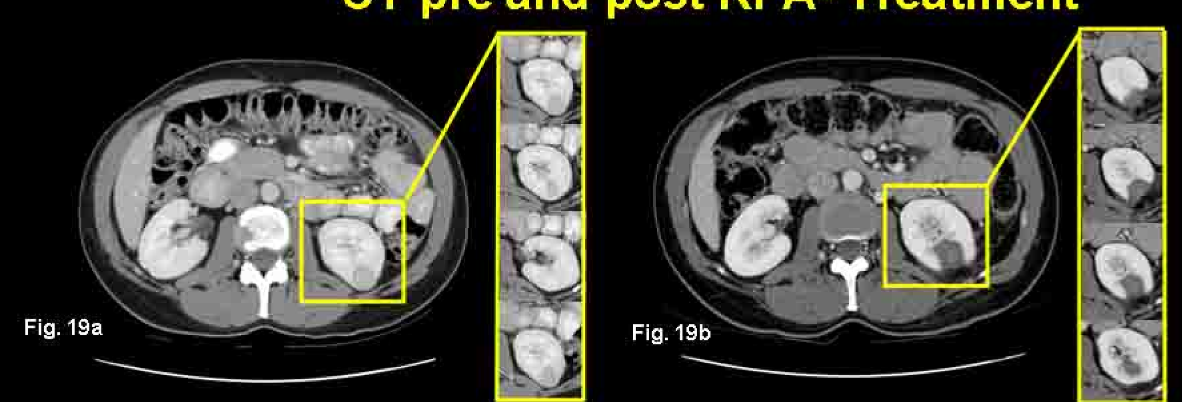


Fig. 16a-c: Pre and post CT scans as well as image fusion to define margins. **Fig. 17**: Fusion of surface displays (pre and post CT) shows 3D relation of tumor to treatment margins. **Fig. 18**: CT - PET fusion diagnoses residual tumor (RT) after RFA which could be visualized by surface rendering based on CT data (Fig. 17).

CT pre and post RFA- Treatment



Figs. 19a,b : Renal cell carcinoma before and after RFA. Conventional imaging makes interpretation by mental registration. Image fusion of the two data sets using the optimized automated registration and adequate colorizing (Fig. 19c) clarifies and defines the treatment margins. Image fusion can be done with the patient still on the table.

Pre and Post Treatment Elastic Fusion

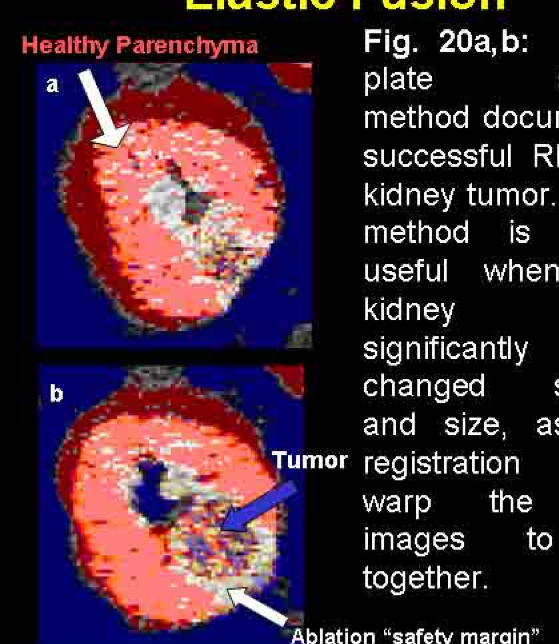


Fig. 20a,b: Thin-plate spline method documents successful RFA in kidney tumor. This method is more useful when the kidney has significantly changed shape and size, as the registration will warp the two images to fit together.

MRI pre RFA for Lesion detection - CT post RFA margin definition

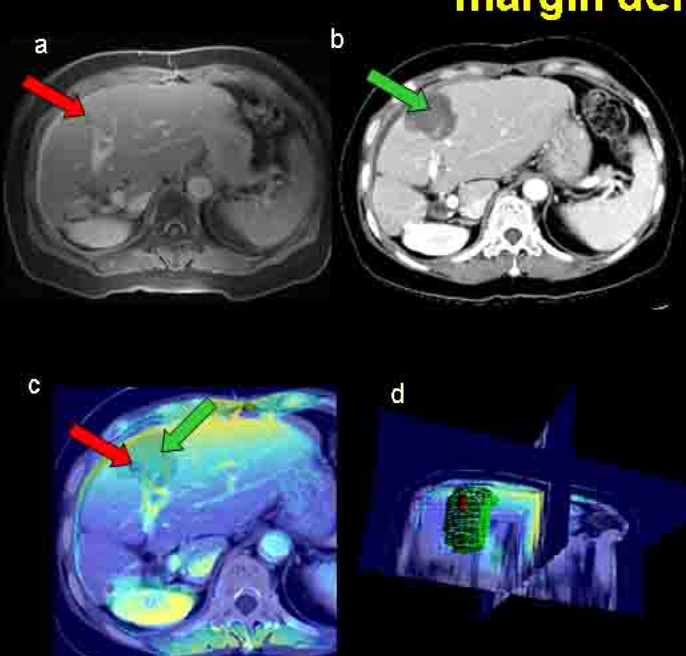


Fig. 21a-c: Pre- and post-treatment fusion images of a solitary hepatocellular carcinoma using the least squares method. This lesion was invisible on CT pre-RFA. The MRI was used to guide needle placement. (a) MR of tumor (arrow) before RFA. The CT (b) of RFA zone (arrow) after treatment. CT (c) to MR fusion demonstrates the ablation margins; notice that the tumor (yellow arrow) is within the kill zone (orange arrow). Three-dimensional rendering (d) of ablation zone (green) encompassing the tumor (red). This lesion was invisible on CT pre-RFA. The MRI was used to guide needle placement.

Discussion & Conclusions

Image co-registration may assist before, during, and after RFA. Often the morphologic and functional imaging studies provide separate complimentary information. Co-registration of pre- and post-RFA images may provide another window into the often subtle spatial relationships between tumor and post-RFA thermal lesion. Normal interpretation uses mental co-registration; however computer processing may provide a more objective and exact view. Because image fusion has been around for such a long time for rigid structures (brain and bone), many technical details have already been worked out. However, two problems emerged while performing image fusion after RFA

The first problem is inherent to the imaging itself. Image fusion is easily performed on the brain, because the skull is a rigid structure that prohibits any significant movements. Unlike the brain [6], the abdominal cavity is not stationary, and organs can significantly alter their shape and location. These changes can be due to breathing, the position of the patient on the table, organ shift, change in organ shape, the contents of the patient's stomach, and the RFA procedure itself, etc. This miss-registration hampered the fusion process in the kidney and liver.

The second problem encountered was that thermal lesions tends to shrink over time. This is problematic because, upon fusion, the thermal lesion looks smaller than the tumor, making it seem as though the entire tumor was not treated. Since these studies were retrospective, it was known that these patients did not suffer recurrence.

The semi-automated technique was the most feasible for clinical real-time navigation. Versatile fusion software with multiple available methods of rigid and elastic fusion may improve chances for optimal fusion for a given patient, as each method has weaknesses that may be unpredictable.

Further validation is indicated before these techniques can be routinely utilized or applied to navigation systems or treatment planning software.

REFERENCES

1. Coreia, JA, et al.: Registration of nuclear medicine images. *J Nucl Med* 31:1227-1229, 1990 (editorial)
2. Maintz, JB, et al.: A survey of medical image registration *Med Image Anal* Mar;2(1):1-36, 1998.
3. Turkington, TG, et al.: Accuracy of registration of PET, SPECT and MR images of a brain phantom. *J Nucl Med* 34:1587-1594, 1993.
4. Pietrzyk U et al.: An interactive technique for three-dimensional image registration: validation for PET, SPECT, MRI and CT brain studies. *J Nucl Med* 35:2011-2018, 1994.
5. Katyal S, et al.: Fusion of immunoscintigraphy single photon emission computed tomography (SPECT) with CT of the chest in patients with non-small cell lung cancer *Cancer Res* 55:5759s-5763s, 1995.
6. Israel, O. et al.: The fusion of anatomic and physiologic imaging in the management of patients with cancer. *Sem in Nuc Med*, 31(3): 191-205, 2001.
7. Wood, BJ. et al,: Percutaneous tumor ablation with radiofrequency. *Cancer*, 94 (2): 443-451, 2002.
8. Jiao-LR et al Clinical short-term results of radiofrequency ablation in primary and secondary liver tumors *Am J Surg*. 177(4):303-6, 1999.
9. McAuliffe MJ et al, IEEE CBMS, 2001, 381-386.
10. Arun KS, et al.: Least squares fitting of two 3D point sets. *IEEE Trans. Pattern Anal. Machine Intell.*, 9: 698-700, 1987.
11. Bookstein FL et al. Principal warps: thin-plate splines and the decomposition of deformations. *IEEE Trans. Pattern Anal. Machine Intell.*, 11(6): 567-585, 1989.
12. Jenkinson M, et al. A global optimization method for robust affine registration of brain images. *Medical Image Analysis*, 5(2):143-156, 2001.
13. Studholme C, et al: An overlap invariant entropy measure of 3D medical image alignment, Pattern Recognition, 32: 71-86, 1999.

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