

Applications of Technical Fusion in Uroradiology

Einsatzmöglichkeiten der technischen Fusion in der Uroradiologie

Authors

F. Aigner¹, T. De Zordo¹, L. Pallwein-Prettner², D. Junker¹

Affiliations

¹ Radiology, Medical University Innsbruck, Austria

² Radiology, Sisters of Charity Hospital, Linz, Austria

Key words

- fusion imaging
- targeted biopsy
- ultrasound
- prostate cancer
- renal lesion
- contrast enhanced ultrasound

Abstract

Technical fusion is defined as the ultrasound-guided navigation through a previously generated 3D imaging dataset such as a computed tomography (CT) or magnetic resonance imaging (MRI). This technique allows for moving the fused CT/MRI datasets synchronously with the real-time ultrasound in the same plane. Established and furthermore not yet described applications, the technical principles and the limitations of this promising technique will be introduced.

Key points:

- ▶ improves detection rates of lesions on ultrasound
- ▶ more reliable size controls at different time points
- ▶ may be an alternative to in bore biopsies
- ▶ can be used for focal therapy

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Zusammenfassung

Unter technischer Fusion versteht man das ultraschallgeführte Navigieren durch einen zuvor generierten 3D-Bildatensatz wie beispielsweise einer Computertomografie (CT) oder Kernspintomografie (MRT). Diese Technik erlaubt es, die in das Ultraschallgerät eingespielten CT/MRT-Datensätze simultan mit dem durchgeführten Echtzeitultraschall zu bewegen, nachdem selbe Schichtpositionen anhand bestimmter anatomischer „Landmarken“ registriert wurden. In der vorliegenden Arbeit werden etablierte, aber auch noch nicht beschriebene Einsatzmöglichkeiten, die Technik und die Limitationen dieser

interessanten Methode auf dem Gebiete der Uroradiologie beschrieben.

Introduction

Currently the radiologist's clinical practice is generally structured as follows: if a lesion previously detected via computer tomography (CT) or magnetic resonance imaging (MRI) and is also monitored using ultrasound (US) should be reevaluated or biopsied, the examiner first examines the static CT or MRI data records on an imaging console in order to get a solid impression of the morphology and localization of the lesion. In the subsequent ultrasound examination, information is recalled from memory in order to find the lesion and characterize it, for example. This approach is called visual or cognitive fusion (CF).

In contrast, technical fusion (TF) allows not only the simultaneous display of real-time ultrasound images with the previously obtained CT or MRI data records on the same screen, that is, on the split-screen ultrasound monitor, but also supports the synchronous movement of the real-time ultrasound image together with the recorded 3D data records using co-registration. In the recent past, the following advantages, among other things, have been ascribed to TF: Discovery of lesions that could not be detected, or were difficult to detect using ultrasound [1]; More reliable, non-examiner-dependent size tracking of various lesions [2]; Targeted biopsies of the prostate or breast [3], which then could be performed in private practice for example, by urologists themselves as a first-line invasive diagnostic procedure.

This overview article will describe the technology of TF, discuss established uses of fusion imaging in uroradiology, such as prostate

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Correspondence

Dr. Friedrich Aigner
Radiology, Medical University Innsbruck
Anichstrasse 35
6020 Innsbruck
Austria
Tel.: ++43/5 12/50 48 20 91
Fax: ++43/5 12/50 42 48 23
friedrich.aigner@uki.at

biopsy, as well as present new, yet unestablished or unevaluated procedures, such as fused imaging of kidneys and the retroperitoneal region for monitoring tumor development. In addition, the limitations of this technology will be critically evaluated.

Technology

Prerequisites

The following 3 components are required to perform technical fusion: 1. An ultrasound unit with fusion software; 2. Sensors attached to the ultrasound probe; 3. A transmitter generating a low magnetic field (► Fig. 1).

Procedural steps

First the 3 D image data sets are uploaded to the ultrasonic instrument, e. g. via an external data medium such as a USB stick or locally from the database. Next is a slice comparison between the B image and 3 D data set for the position at which certain landmarks can be detected in both modalities (e. g. bladder neck during prostate fusion) (► Fig. 2). If the comparison is satisfactory, the fusion mode begins.

Principle

In fusion mode, the transmitter three-dimensionally localizes the position of the sensors attached to the ultrasound probe and continuously sends their coordinates to the ultrasound unit. In this way the 3 D data record can be moved simultaneously with the real-time ultrasound examination on the monitor of the ultrasound unit (► Fig. 1). In addition, the system transfers designated targets to the 3 D data record of the examination to be fused; these targets appear directly on the live ultrasound image.

Prostate



Due to the deficiencies of systematic biopsy (SB) and the PSA value for diagnosing prostate cancer, visualization of the prostate carcinoma (PCa) is playing an increasingly important role in diagnosis [4, 5]. In particular, MRI appears to be a stable technology, and in contrast to transrectal ultrasound (TRUS), is reproducible independently of the examiner [6].

Initially in the biopsy setting, in addition to systematic tissue cores, targeted samples were acquired via cognitive fusion of suspicious areas identified in the MRI; in such cases, a suspected lesion in the MRI is attributed as exactly as possible to a topographical region; TRUS is then performed in this area, and subsequently additional tissue samples are obtained. A recently published study by Boesen et al. emphasized the diagnostic value of CF, even when – as in this case – the authors had little experience with MRI-guided biopsies [7]. Their study population consisted of 83 males with earlier negative systematic prebiopsies who also underwent both SB and an MRI-targeted biopsy using CF. Consequently they achieved a total PCa detection rate of 47% for the combined systematic biopsy and cognitive fusion approach, while CF detected an additional 13% clinically significant cases of PCa that had eluded systematic biopsies alone.

Therefore urologists in private practice are increasingly desirous of exact localization data of MRI findings so that in their practice they can obtain additional tissue samples from these regions.

In order to counteract possible MRI image information loss via CF, some working groups started to perform MRI-guided biopsies in magnetic resonance scanners (so-called “in-bore” biopsies) [8]. This procedure is currently reserved for a few centers with the appropriate equipment.

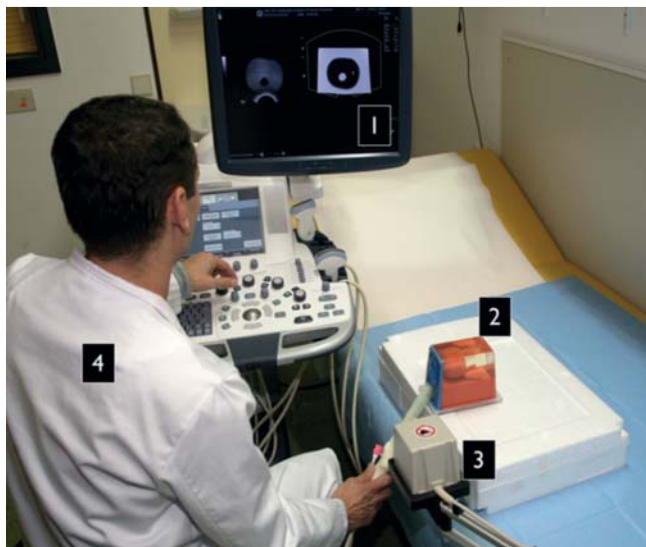


Fig. 1 Setting of fusion imaging with split screen (1 real-time TRUS on the left and MRI data set on the right), prostate phantom 2, transmitter near the sensors on the probe 3 and investigator 4.

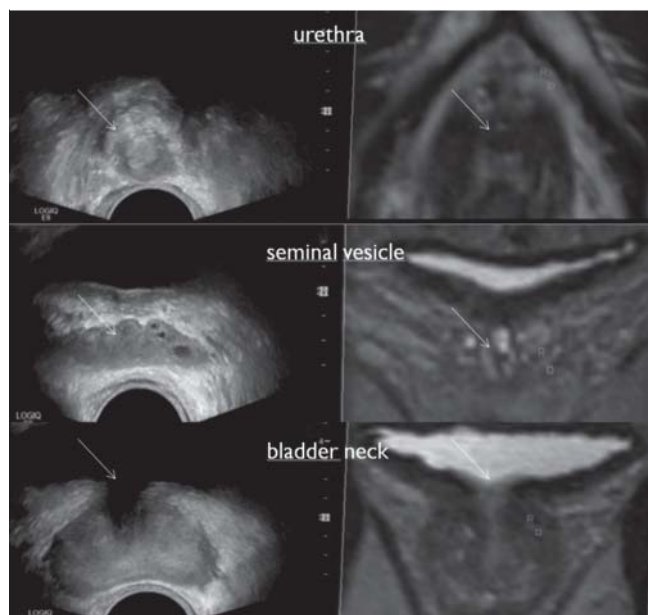


Fig. 2 Because urethra, seminal vesicle or bladder neck are visible on both MRI and ultrasound they may be used as reference points for slice registration.

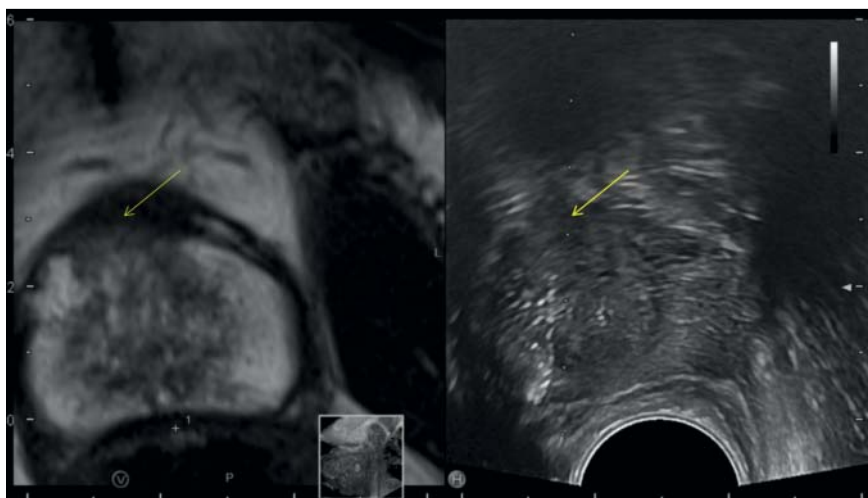


Fig. 3 MRI/TRUS fusion-targeted biopsy of a cancer suspicious area on MRI (arrows) in an anterior location of the prostate; histology revealed a Gleason 7 prostate cancer.

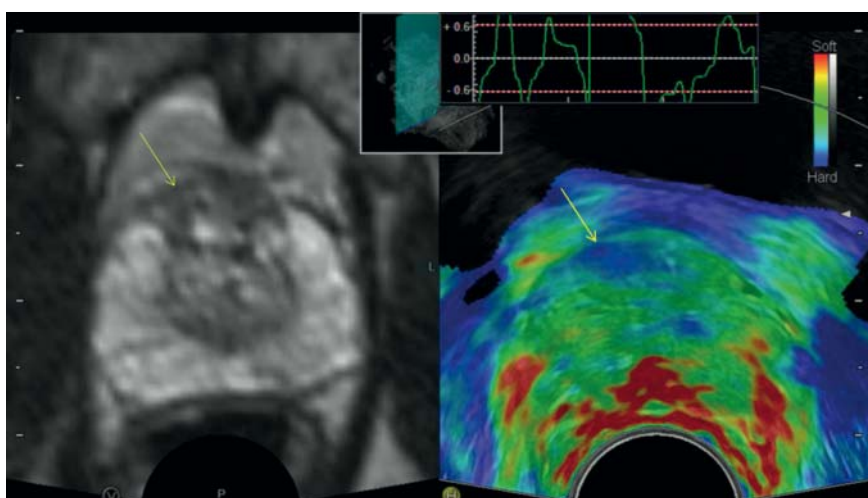


Fig. 4 Reevaluation of a cancer-suspicious area on MRI (arrow; left image) with ultrasound elastography (arrow; right image); note that the area is colour-coded blue on elastography indicating increased tissue stiffness.

In this regard, the possibilities offered by technical fusion are increasingly interesting, since after the MRI data sets have been uploaded to the ultrasound device, the suspected lesion can be biopsied by radiologists and urologists using TRUS independently of large-scale equipment (◉ Fig. 3). In addition, TF combines the advantage of two imaging procedures, real-time TRUS and MRI. However, this requires close collaboration and communication between the urologist and radiologist. Wysock et al. reported the comparative advantages of TF over CF with respect to prostate biopsies: 1. TF reduces the learning curve for CF; 2. More histological information is made available; 3. TF improves the detection of small carcinomas [3].

An additional useful option offered by technical fusion mode is that, in addition to ultrasound-guided selection of the MRI-targeted lesion in the B image, reevaluation of the suspected MRI lesion is made possible using new ultrasound techniques such as ultrasound elastography or contrast-enhanced ultrasound (CEUS) [9, 10]. Thus Brock et al. reported improved visualization of PCa when the strengths of MRI and ultrasound elastography can be simultaneously combined [9]. Further, Durmus et al. were able to achieve good focus characterization with parallel employment of a

B image, ultrasound elastography, color Doppler, CEUS and MRI [10] (◉ Fig. 4).

In general, compared with SB, the following advantages of an MRI-guided biopsy should be emphasized: (1) Better estimation of the actual tumor load; (2) Detects more clinically significant prostate cancers; (3) Requires fewer tissue cores for tumor verification; (4) Detects fewer indolent prostate cancers; (5) Indicates prostate cancer in difficult cases of localization [7, 11, 12]. Due to these advantages, technical fusion also appears to be suitable for patients in active surveillance [13].

Kidneys

Identifying renal lesions

Due to reasons of cost and radiation-reduction purposes, frequently in cases of unclear CT or MRI findings a second-look B image ultrasound examination (B-US) is performed to obtain additional clarification of various lesions. For incidental enhancing breast lesions in a contrast-enhanced MRI, Nakano et al. showed that using technical fusion of the B-US is not only more independent of the examiner, but also that the detection rate of these lesions using TF is

significantly higher than for those relying on cognitive fusion (83% for TF vs. 30% for CF) [1].

The same appears to apply to the discovery and characterization of indistinct renal lesions previously detected by a CT or MRI. Thus Helck et al. were able to demonstrate that using technical fusion provided significantly improved identifiability of renal lesions, compared to B-US alone (2.7 ± 1.2 vs. 2.0 ± 1.3) [14]. Interestingly this also applies to CEUS which in the same study likewise more reliably discovered renal lesions using technical fusion (CEUS-TF). An analysis of 29 consecutive renal lesions at our institute confirmed the results of the above study, whereas in our cohort the identifiability of lesions for sole B-US was 44.8% and 86.2% for TF ($p = 0.002$) (unpublished data).

Characterizing renal lesions

Unclear CT or MRI findings for renal lesions can result from e.g. purely monophasic examinations (due to contrast agent dynamics?), in the case of minimal contrast agent absorption (partial volume effect? septal enhancement?), or in the case of the presence of hemorrhagic renal cysts in the MRI [14–16]. If such an indistinct renal lesion has been successfully discovered by means of the fusion mode, an ultrasound contrast agent can be applied to further characterize the lesion. Due to the high sensitivity of CEUS, this technology possesses great potential in the differentiation of solid and cystic renal lesions, differentiating solid renal lesions and pseudotumors as well as characterizing complex cysts [16–23]. In their study population, Helck et al. demonstrated the superiority of CEUS-TF compared to CT/MRI exami-

nations in the characterization of renal lesions [14]. **Fig. 5** shows a patient from our cohort for whom only a monophasic CT was available, and who did not require additional examinations due to the CEUS-TF.

Radiofrequency ablation

Recently published studies of ablation of liver lesions indicate that the use of technically fused radio frequency ablations under real-time conditions is technically possible, safe and efficient. Thus, in many cases, technical fusion could be employed as alternative to CT-guided ablation [24, 25]. Unlike liver studies, there is little literature regarding fusion-guided renal intervention, although study groups followed by Ukimura and Amalou demonstrated that this is technically feasible [26, 27].

Follow-Up

Size controls

In principle every 3D-reconstructible DICOM image data set can be used for fusion imaging. This means that in addition to CT/MRI data sets, PET-CT volumes or so-called TRUE 3D ultrasound volumes created using fusion imaging techniques could be employed. Thus Nakano et al. initially created a US-3D data set for BI-RADS 3 lesions of the breast which they then used for size progression controls (6, 12, and 24 months) in fusion mode for comparison with the real-time ultrasound image [2]. The primary diameter of the lesions initially and after 6, 12 and 24 months was indi-

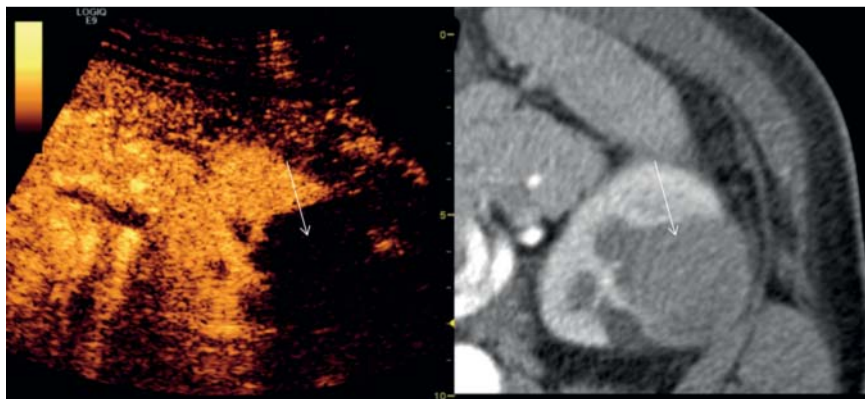


Fig. 5 CEUS-TF: high-attenuation lesion of the kidney on monophasic CT (arrow; right image) with absence of contrast agent uptake on CEUS (arrow; left image); therefore cancer could be ruled out.

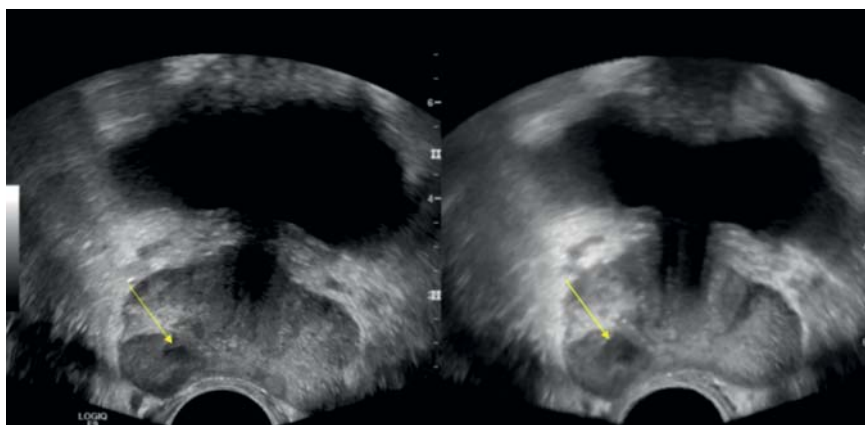


Fig. 6 Fusion of real-time ultrasound (left image) and TRUE-3D-US data set generated 10 days before (right image); follow-up shows the absence of the prostate with a smaller size.

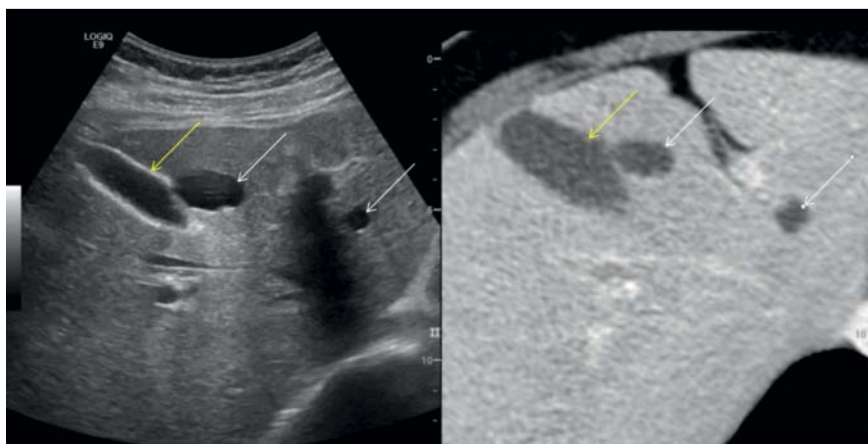


Fig. 7 Good slice correlation between real-time ultrasound (left image) and a 6-month-old CT data set (right image); note that the gallbladder (yellow arrow) and 2 hepatic cysts (white arrows) are in the same plane.

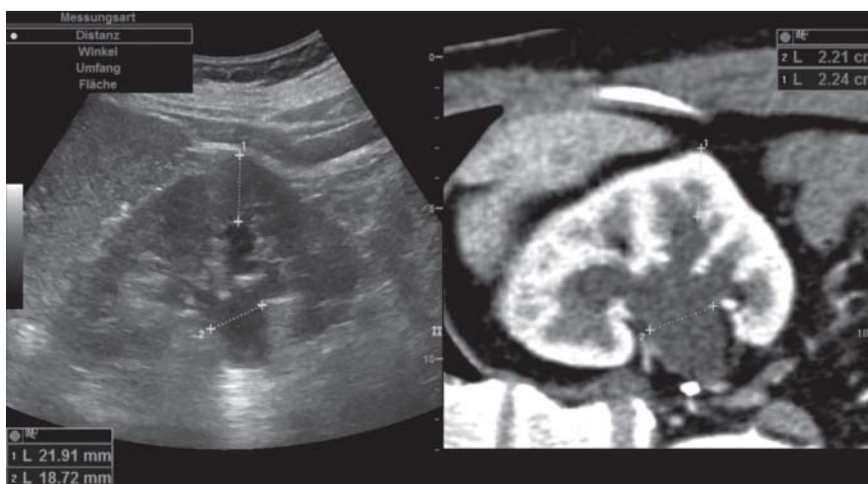


Fig. 8 Follow-up of a UPJ stenosis surgically treated in 1999; real-time ultrasound of 2014 (left image) fused with a CT data set from 2008; no loss of parenchyma and no growth of dilatation visible.

cated to be 8.2 ± 4.2 , 8.4 ± 4.5 , 8.1 ± 4.5 and 8.3 ± 5.0 mm ($p=0.785$). The authors concluded that using TF, BI-RADS 3 lesions could be reliably reproduced at various points of time, independent of the examiner.

We employ US/TRUE 3D-US fused examinations for size progression monitoring of e.g. renal lesions, prostate abscesses or verified PCa for patients under active surveillance. **Fig. 6** illustrates one of our patients with a prostate abscess for whom we initially established a US-3D volume, and whom we monitored 10 days later using TF.

However, technical fusion also demonstrated its value for the following issues, and is therefore used routinely in this regard.

Restaging

US/CT-TF can be used for restaging of e.g. seminoma patients in the course of ultrasound progression monitoring months after an initial CT scan as a supplement to a simple B image ultrasound. This offers greater certainty in the assessment of ambiguous changes, during the discovery of sonographically difficult to detect changes (e.g. retroperitoneal lymph nodes), or in cases of size progression evaluation such as described by Nakano et al. [2] (**Fig. 7**).

Additional applications

Technical fusion can prove useful for more independent progression assessment of e.g. nephropyloplasty (**Fig. 8**),

prostate volume and abscesses, renal trauma (**Fig. 9**), or ureteral calculus.

Limitations

As a rule, the purely technical aspects of TF present no difficulty after a short learning phase [2].

However, in its current state of development, TF still exhibits a few shortcomings and imprecision. In addition to the general limitations of ultrasound such as the presence of fat deposits, non-compliance or overlying bowel gas [14], the following difficulties are specifically related to technical fusion. First, the majority of currently available ultrasound units with integrated TF functionality have not been able to compensate for inaccuracies resulting from breathing movements or deformation of organs or body parts. Thus if a CT or MRI of the abdomen has been generated during deep inspiration, it can be difficult to achieve the same breathing position during the ultrasound examination. Additional problems can occur during an MRI/TRUS-TF of the prostate, since the organ is deformed as a function of the pressure applied by the TRUS probe. Further, movements of the probe displace the prostate. Currently, these inaccuracies can be only cognitively offset by good anatomical familiarity and sufficient practice by the examiner. This can be made somewhat easier on new instruments by the possibility of re-

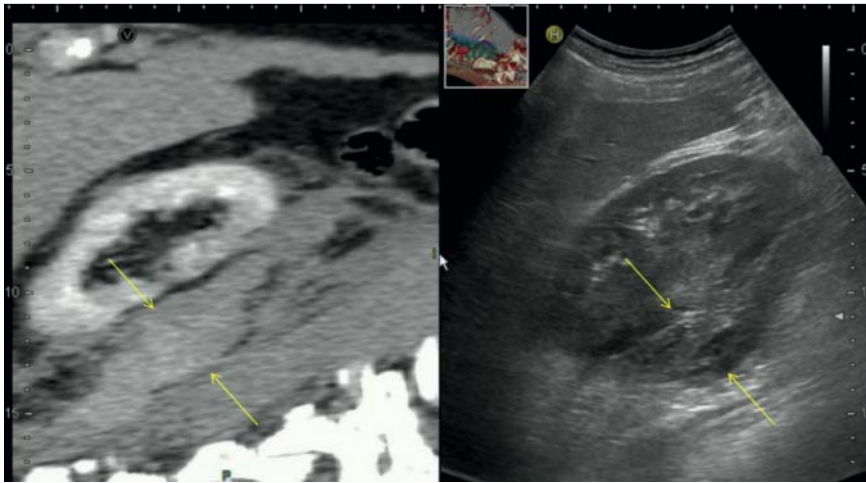


Fig. 9 Follow-up of a perirenal hematoma caused by trauma of the right kidney (arrows); no enlargement of the hematoma on real-time ultrasound (right image) several days after accident in comparison with the initial CT data set (left image).

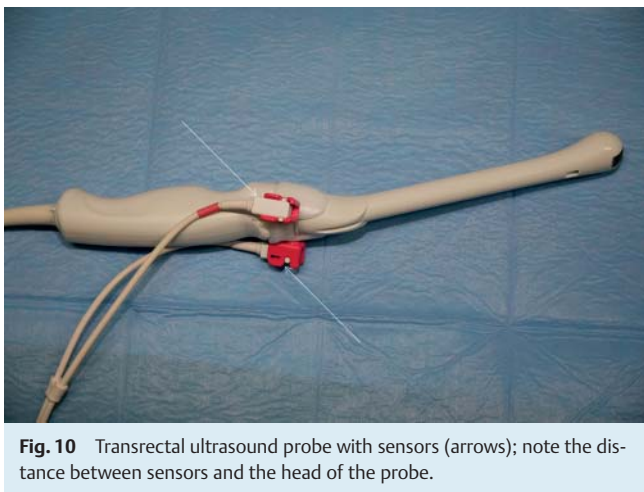


Fig. 10 Transrectal ultrasound probe with sensors (arrows); note the distance between sensors and the head of the probe.

Recording different images in various layer positions, respiration positions or varying contact pressure, then accessing them later. With respect to deformation and intracorporeal movement of the prostate, Schilling et al. suggested applying constant contact pressure as well as multi-point registration [28]. Software which can compensate for inaccuracy caused by e.g. organ deformation would be desirable for genuine technical fusion after proper image recording. It should be further considered that when using an endfire TRUS probe, other layer angles are generated in the ultrasound image, in comparison with MRI depending upon the angle of inclination [29].

Another source of TF imprecision is posed by the attachment and placement of the position sensors on the distal grip of the ultrasound probes made by most manufacturers. In particular, when long ultrasound probes such as the TRUS probe (► Fig. 10) are used, the movement areas of the end of the transducer which generates the real-time US images differ from the sensors coupled to the movement of the 3D image data sets. Multi-point registration would be a means to a solution; however, ultrasound probes with sensors already integrated into the end of transducer would be a desirable improvement.

Currently it is difficult to provide an exact quantification of registration errors/deviations in millimeters for TF, since a

wide variety of software platforms are used (rigid, elastic, electromagnetic needle tracking) as well as biopsy types (transperineal, transrectal), and in addition, there is insufficient published data regarding the precision of technical fusion (particularly for biopsies) [30]. Pokorný et al. report that a registration precision of 3.1 mm would be required to hit a 1 cm large lesion with 95% probability on the initial examination [31]. Ukimura et al. achieved a deviation error of 2.92 mm as well as a success rate of 84% using a 3-dimensional elastic registration system on a prostate phantom with integrated tumor clusters [32].

Finally, most manufacturers offer fusion software only for premium-segment ultrasound units, which has an indirect effect of making technical fusion relatively expensive.

Conclusions

The use of technical fusion in urology opens numerous possibilities and simplifications. TF-guided biopsies and ablations of the prostate, for example, are a possible alternative to interventions guided by large-scale equipment especially in the private urological practice, offering examiner-independent therapy monitoring as well as the identification of changes difficult or impossible to detect using only B image ultrasound. Affordable ultrasound units and technical developments would be desirable.

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