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PHYSICS CONTRIBUTION

DEDICATED MAGNETIC RESONANCE IMAGING IN THE RADIOTHERAPY CLINIC

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Purpose: To introduce a novel technology arrangement in an integrated environment and outline the logistics model needed to incorporate dedicated magnetic resonance (MR) imaging in the radiotherapy workflow. An initial attempt was made to analyze the value and feasibility of MR-only imaging compared to computed tomography (CT) imaging, testing the assumption that MR is a better choice for target and healthy tissue delineation in radiotherapy.

Methods and Materials: A 1.5-T MR unit with a 70-cm-bore size was installed close to a linear accelerator, and a special trolley was developed for transporting patients who were fixated in advance between the MR unit and the accelerator. New MR-based workflow procedures were developed and evaluated.

Results: MR-only treatment planning has been facilitated, thus avoiding all registration errors between CT and MR scans, but several new aspects of MR imaging must be considered. Electron density information must be obtained by other methods. Generation of digitally reconstructed radiographs (DRR) for x-ray setup verification is not straight forward, and reliable corrections of geometrical distortions must be applied. The feasibility of MR imaging virtual simulation has been demonstrated, but a key challenge to overcome is correct determination of the skeleton, which is often needed for the traditional approach of beam modeling. The trolley solution allows for a highly precise setup for soft tissue tumors without the invasive handling of radiopaque markers.

Conclusions: The new logistics model with an integrated MR unit is efficient and will allow for improved tumor definition and geometrical precision without a significant loss of dosimetric accuracy. The most significant development needed is improved bone imaging.

MR, MRI, radiotherapy, workflow.

INTRODUCTION

Radiation therapy includes a series of procedures, including therapy planning, treatment delivery, and therapy adaptation during the course of treatment and follow-up. In all these steps, different types of imaging are involved. The most common imaging techniques today are based on radiogaphy and computed tomography (CT). Magnetic resonance (MR) imaging has so far not managed to replace CT in treatment planning partly due to technical challenges such as the presence of image distortions, the lack of electron density information required for dose calculations, and poor bone imaging. However, MR as a complement to CT for target delineation has become more common. In most cases, this procedure is performed by anatomical registration of the MR images to a treatment planning CT scan.

The obvious value of MR imaging compared to that of CT is the improved contrast resolution between different types of tissues that, in many cases, cannot be resolved by CT. Superior characteristics in outlining tumors and organs at risk for a number of clinical sites has been demonstrated, *e.g.,* brain lesions (1), critical organs in the head–neck region (2), tumor bed localization for partial breast treatment (3), and cervix (4), prostate (5), and rectum (6). Studies of MR-assisted treatment planning in gynecological cancers indicate improved local control and minimal treatment-related morbidity (7). More precise tumor localization and staging in colorectal

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cancer treatment was achieved with axial T_2-weighted MR imaging (8).

For obvious reasons, there are very few comparisons where the actual tumor extension is known and can be used as a reference. Another quality parameter may be the ''interobserver variation,'' when tissue segmentation has been performed with both MR and CT imaging. For example, for central nervous system tumor delineation, the use of a combination of MR/CT was shown to significantly reduce the interobserver variation (9). Delineation of the prostate based on CT imaging has been shown by a number of groups to differ significantly compared to that of MR, with respect to both the mean size and the interobserver variation (10). For head–neck tumors, a slightly decreased interobserver variation was found for some organs at risk with MR imaging, but no significant difference for tumor delineation was observed (11).

An important consideration in using MR registered to CT is the inaccuracy in image registration procedure, which may introduce further errors in target localization (12).

Currently, a high-precision treatment setup of soft tissue tumors is often performed by x-ray imaging after insertion of radiopaque markers or by CT imaging methods. The CT methods do not require any invasive procedure, but because of inherently low soft tissue contrast, these images always require a trained expert to be actively involved in the therapy delivery workflow. Even expert delineation of organs such as the prostate based on CT imaging alone has been demonstrated to give rise to substantial interobserver variations (10). A convenient utilization of MR at treatment delivery, however, would require either a specially combined MR and linac MR-linac (13, 14) or an efficient transport solution as suggested by Karlsson *et al* (15) for high-precision proton therapy.

Geometrical distortions in MR scanners are the result of nonlinearity of the gradient fields, intrinsic inhomogeneity in the main magnetic field or they are induced by the patient. The spatial accuracy will also, generally, decrease toward the periphery of the patient. In modern MR scanners, the nonlinearity can be corrected by using algorithms provided by the MR scanner manufacturers. A number of groups have demonstrated the feasibility of using MR for treatment planning when distortions are properly accounted for by careful selection of MR sequences and application of adequate corrections for the remaining inhomogeneities (16–18).

MR images do not carry information about the electron density needed for treatment planning. A number of groups have shown that this can be overcome to a large extent by setting only three bulk electron density values to segmented bone, air/lung, and tissue. Lee *et al*. (16) have demonstrated that the use of a 1.5-T MR scan would create dosimetric uncertainties of less than 2%, and similar data were presented by Chen *et al*. (12) for a 0.23-T MR. Prabhakar *et al*. (1) investigated the dosimetric consequences of using MR only for brain tumor treatment planning and concluded that MR-based treatment planning for brain lesions gives dosimetric results that are equivalent to those of CT-based treatment planning.

The purpose of the present project was to develop a new workflow and demonstrate a fully integrated MR imaging solution for radiation therapy. Expected advantages with this new concept include improved tissue contouring, improved precision in soft tissue therapy setup, biological information at treatment planning, and imaging of therapy response. The suggested MR procedure should further result in less redundant imaging and be more cost effective. By replacing x-ray procedures with MR imaging, an additional benefit of reducing the ''out-of-target dose'' would also be possible for cases in which this may be an issue.

METHODS AND MATERIALS

Technologies

The building at University Hospital of Umeå was prepared for the installation of an MR scanner in close proximity to one of the clinical accelerators (Fig. 1). A radiation-shielded door between the MR scanner and the accelerator allows for direct transportation of the patient between the MR scanner and the accelerator while the patient is still immobilized within a fixation apparatus.

The MR imaging is performed with a 1.5-T Siemens Espree unit, and for radiation therapy, a dual-energy (6-MV and 15-MV) linear accelerator equipped with multi leaf collimator and an MV portal imager (Siemens ONCOR unit with Optiview) is used. The standard radiofrequency coils in the MR scanner are used for all treatment sites located below the neck. A special bridge (coil holder) has been developed to avoid deformation of the patient surface during the MR scanning. To allow for adequate fixation of head-and-neck patients, a system with a bridge combined with flexible coils is evaluated. A typical protocol for target delineation includes high-resolution images with appropriate contrast (typically T_2 for the pelvic region and T_1 for brain when gadolinium contrast is used). For treatment planning, a T_2-weighed three-dimensional (3D) sequence that covers the patient's outer contour is used.

All fixation devices have been chosen and modified to be MR compatible, i.e., all metal parts have been removed and the use of carbon fiber is avoided in the vicinity of the patient. The 70-cm-diameter bore of the MR scanner is similar to that of most CT units,

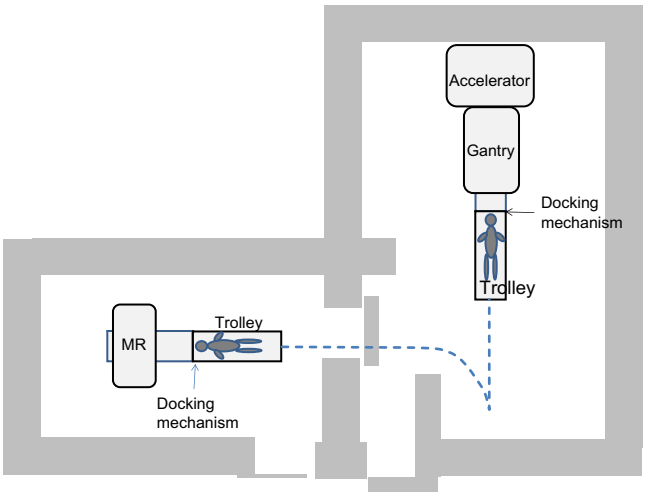

Fig. 1. Radiotherapy building with the MR and the connected accelerator.

and thus, no further modifications of CT-compatible fixations are required.

The transport trolley is a standard Siemens Myabi trolley used for image-guided surgery, with a special docking device added to the therapy table (Fig. 2). The patients are transported between the MR scanner and the accelerator on top of a thin sliding board (14 mm thick with 3% photon attenuation at 15 MV and 4.5% at 6 MV). During this transport, the patients are immobilized with a double vacuum device (Body fix from Medical Intelligence) fixed to the sliding top by four tabs. The fixation system is used at both the MR scanner and the accelerator. The system has been locally verified for use in MR, with special restrictions for the vacuum pump.

The equipment added for virtual MR simulation consists of a modified laser bridge (LAP) connected to a prototype implementation of a *syngo* Dosimetrist virtual simulation workstation.

An on-board portal imaging system (Optivue) is used for verification of patient position with orthogonal 2D MV images. This system is also capable of acquiring 3D MV cone beam imaging using MVision™. A version of an ultra-short echo time sequence (UTE) currently under development has been used to test the potential for enhancement of bone in MR images (19, 20). Images with echo times of 0.07 and 4.76 ms were used.

Procedures

The design of this new workflow assumed that all accelerators in the department are equipped with either MV or kV imaging devices, so that conventional simulators for verification of isocenter and beam arrangements are avoidable. It was furthermore assumed that so-called virtual simulation with CT or MR can replace the conventional simulator for all patients.

Figure 3 shows the intended set of procedures and workflow for treatment planning and position verification of the patient. The upper part of the figure illustrates the planning procedures and the lower part the treatment delivery. The planning based on MR data could go either through a treatment planning system or, for easier cases, through virtual simulation.

Morphological imaging for treatment planning will generally be performed by two linked scanning protocols, with the patient in the same geometry and the coordinate system kept constant. The total scanning time for morphology is typically less than 15 min.

All patients are immobilized and scanned in MR-compatible fixation devices. For soft tissue tumors, for which an MR-supported setup will be used at treatment delivery, the patient is oriented and immobilized in a vacuum support which is firmly attached to the movable Myabi top. This top is firmly fixed to the coordinate system of the MR at imaging and to the coordinate system of the accelerator at treatment.

For treatment planning, tumor and healthy tissue segmentation is performed on a dedicated *syngo* Oncologist workstation. Currently, the outer contour of the patient is automatically segmented, but segmentation of bone, lung, and air must be done manually until automatic segmentation tools are available. The following treatment planning is performed with a commercial Nucletron Masterplan treatment planning system (version 3.0). This version of the planning system has been modified to import electron density data for structure sets over the DICOM/RT standard, to be used in dose calculations as an alternative to the CT-based Hounsfield units. For dose calculation purposes, the segmented volumes are set to standard mass densities of 0 for air, 0.30 for lung, 1.02 for soft tissue (corresponding to a mixture of adipose tissue and muscle), 1.30 for bone in the pelvic region, and 1.80 for skull bone. The mass densities are within the treatment planning system (Masterplan) mapped to a Hounsfield number, tissue, and finally electron density. This version of the Masterplan system further facilitates viewing treatment plans on top of either CT or MR images. Virtual simulation is performed on a modified *syngo* Dosimetrist workstation.

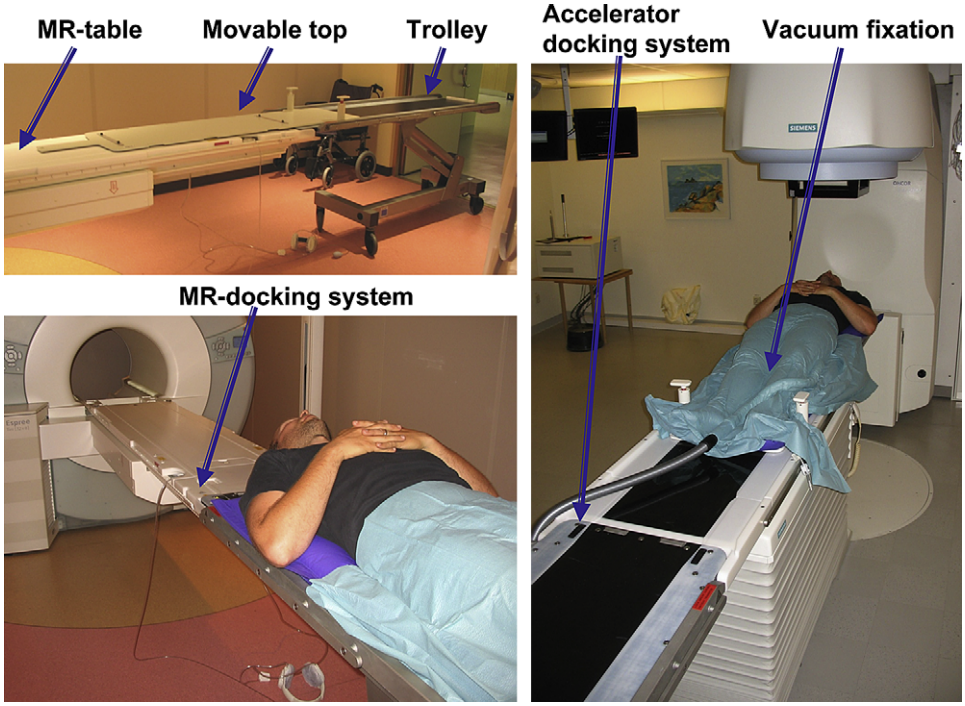

Fig. 2. The trolley solution with a special docking device for smooth and precise transfer between the MR and the accelerator.

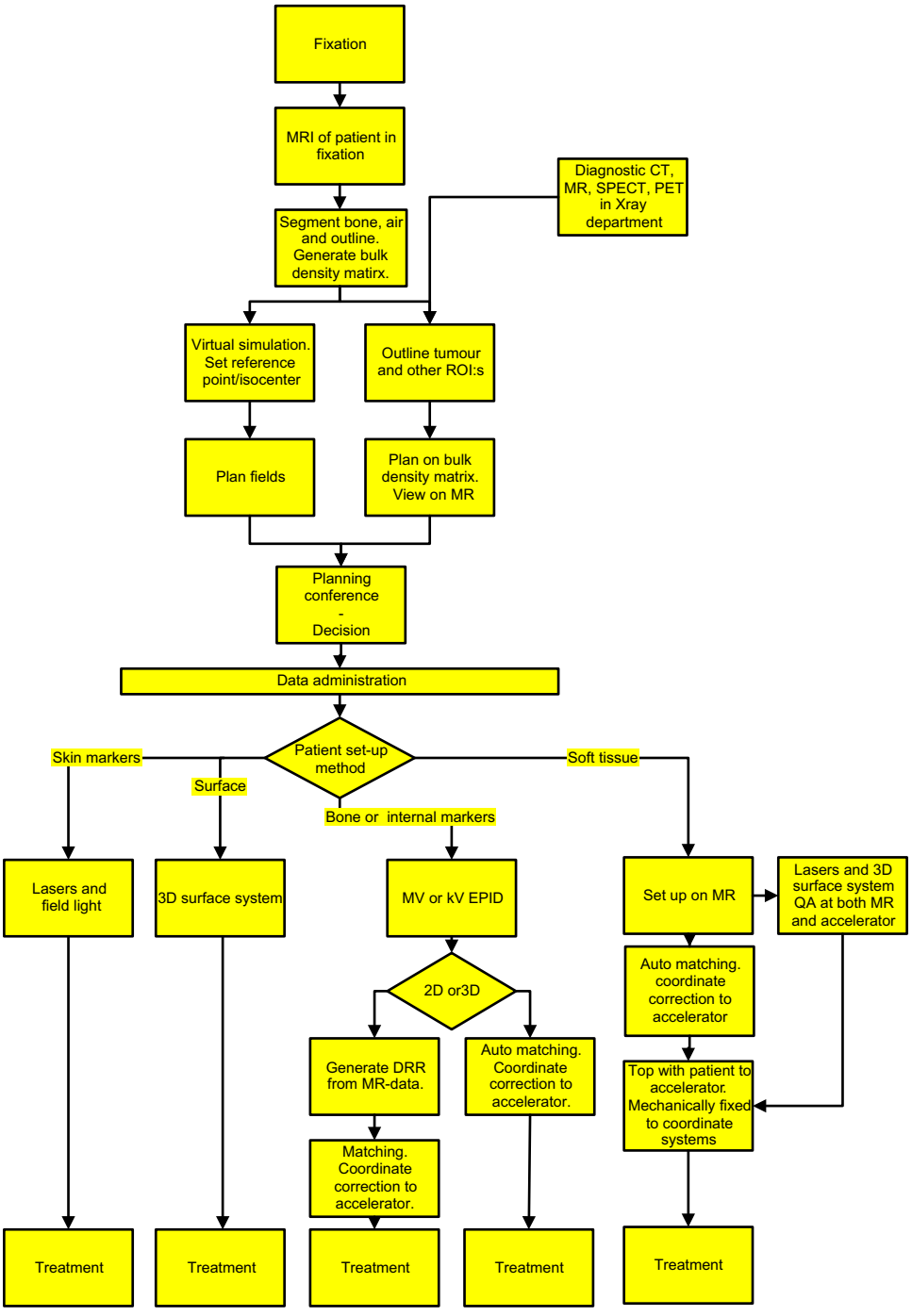

Fig. 3. Proposed radiotherapy process.

The method used for positioning the patient/tumor at each fraction should be based on the goals of treatment and the characteristics of the treatment area. Different patient conditions demand different precision, and different treatment area characteristics require different setup methods. Four different paths through the process have been identified.

Path 1. External markers on the skin should be used where the precision is not of vital importance (*e.g.,* selected palliative treatments).

Path 2. The external surface as reference may be used for cases like breast cancer where the external surface is of major importance. In this case, a 3D positioning system, AlignRT (Vision RT) will be used for setup. Electronic portal imaging may be used in special cases.

Path 3. When bony landmarks or internal markers are used as references, there are in principle two alternative paths. DRRs based on bone imaging with MR or implanted markers localized by MR imaging are matched to orthogonal 2D images from Optivue. In an alternative path, 3D MR images are registered to 3D cone beam images from a kV or MV cone beam systems, using mutual information methods.

Path 4. For mobile soft tissue tumors that demand high geometrical precision, the patient is immobilized at the MR scanner and then transferred to the accelerator for immediate treatment. Setup

of soft tissue tumors will be facilitated by the MR imaging. The treatment coordinates are defined by the absolute coordinates from the treatment planning combined with delta coordinates for the specific treatment session. The positioning MR image is acquired with the same imaging parameters used for the treatment planning MR image (typically a 3D sequence, acquired in less than 5 min). The delta coordinates are obtained through registration of the two image sets. The calculation and transfer of the coordinates to the accelerator control system are done while the patient is transferred in full fixation to the treatment machine (<2 min). The image registration which is the basis for the delta coordinate calculation is currently performed in a prototype software for image fusion. To enable a fully online workflow, the registration will be moved to a workstation with a direct connection to the accelerator. Prior to treatment delivery, an extra security check can be performed by imaging the patient surface with a 3D optical system (AlignRT from VisionRT), which is installed on both the MR and the treatment unit.

RESULTS

Initial experience with an integrated MR scanner in the radiotherapy process suggests that the improved contrast in the images compared to those of CT facilitates safer outlining of the tumor and the healthy tissues to be spared. The prostate is one of the most significant sites where more detailed MR imaging is regarded as superior relative to that of CT (Fig. 4).

In virtual simulation procedures, the skeletal parts are often used to make a quick verification of beam arrangements. In our initial studies of the MR-only concept, we find a number of situations where it is hard to replace bone as the reference structure. Early development of new UTE bone image-enhancing sequences indicates the potential of MR to fulfill this requirement. Figure 5 visually compares slices and DRRs based on CT, T_2-weighted MR images, and a prototype UTE sequence. The UTE sequence shows improved bone visualization but still with enhancement of non-bone structures as well. In the first clinical evaluation, it was concluded that further improvement of the bone visualization was needed to overcome the use of combined MR and CT.

Treatment planning based on MR data will slightly reduce the accuracy in the dose calculations. Initial studies of MR-only treatment planning by using manually segmented bulk densities for tissue, bone, lung, and air indicate deviations of less than 2% compared to those of full CT planning. In this initial stage, all patients were scanned with both MR and CT, but no significant deviations were found in the analyses of geometrical distortions on this clinical material.

Demonstration of the dose distribution on top of MR images (Fig. 6) instead of CT is generally better for visualization of the tumor and healthy tissue in relation to the dose distribution. However, the patient's skeleton has traditionally been used as an internal coordinate system for many purposes. In our initial experience, the lack of bony structures has been regarded as a drawback which must be evaluated over a longer period as more clinical experience with this type of imaging is needed.

Positioning of patients based on soft tissue information with the MR setup procedure at treatment is a noninvasive method. Our initial tests with the new trolley solution (Fig. 2) have proven the feasibility of the concept. The accuracy of the positioning method depends on the reproducibility of the position of the Myabi shell at the treatment and MR table, the spatial stability of the MR isocenter, the image registration accuracy, and the correction for the deflection of the treatment table, which is weight dependent.

The speed of this procedure is heavily dependent on the robustness of the MR-to-MR registration methods and thus the need for manual intervention. For prostate applications, a prototype software for ''prostate-only'' registration was shown to significantly reduce the need for manual intervention in this registration procedure.

At treatment setup, the lack of bone visualization with MR imaging can in some cases be overcome by using volumetric 3D matching. However, in many clinical routines, bony

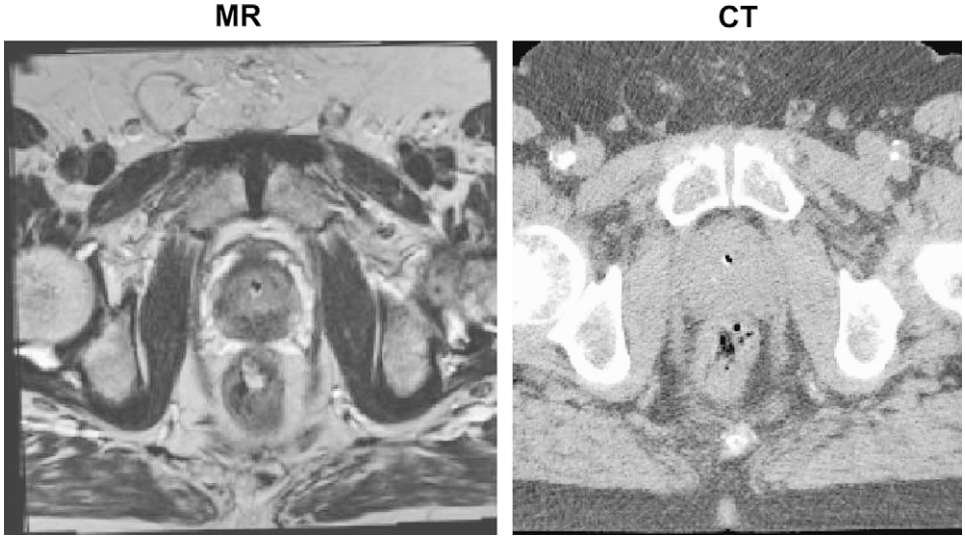

Fig. 4. Illustration of tumor and healthy tissue in the prostate region by MR and CT images.

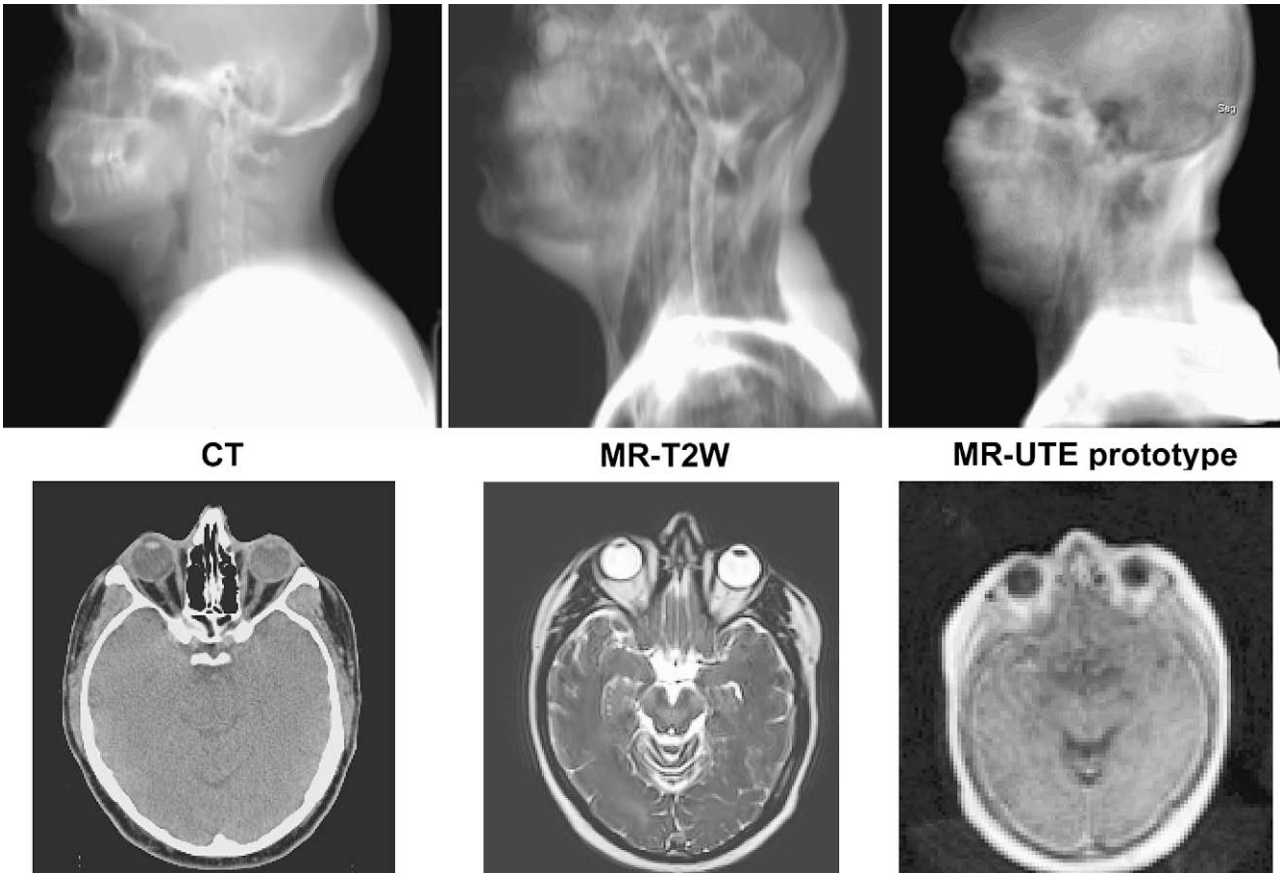

Fig. 5. DRRs and slices based on CT, T_2-weighted MR imaging, and a prototype UTE image. The UTE image is a subtraction of the images acquired with 4.76 ms echo time from the image with 0.07 ms echo time.

landmarks presented in DRRs are needed for setup verification by orthogonal kV x-ray or MV imaging. Current experience verifies the importance of further development of bone imaging by MR in the radiotherapy process.

DISCUSSION

For many categories of patients, the increased geometrical accuracy of MR-based tumor segmentation is believed to compensate well for a slightly reduced dosimetric accuracy. The table currently used for bulk densities will generally result in dosimetric errors of less than 2%. The geometrical distortions reported in early work with MR imaging are not acceptable for radiation therapy. Due to the more recent development in individual magnetic field shimming and advanced 3D correction procedures, these artifacts have been significantly reduced. However, in the site-specific protocols for tumor visualization, optimization for geometrical distortions may have to be compromised. In the ongoing development and clinical evaluation of tumor-specific MR protocols, the significance of these artifacts will be further analyzed.

A four-path selection of setup procedures has been suggested. In an ideal application, the expected uncertainty in each step of the procedure should be analyzed in advance for use in the treatment planning and the radiotherapy prescription. Such data are currently not available, but systematic application of the suggested procedures should actually allow for such uncertainty simulations to be performed as a part of the treatment planning.

An efficient MR imaging procedure for patient setup at treatment of tumors with no fixation to bony structures will reduce the need for invasive methods. This procedure will also allow for both anatomically and biologically adapted radiotherapy without any extra imaging procedures outside the daily routine. Intrafraction organ motion during radiotherapy for prostate cancer has been discussed and analyzed by a number of authors, and a general recommendation is to treat after the patient's rectum has been emptied and to keep the total time between imaging and the end of treatment less than 20 minutes (21). In our concept, the time between MR imaging and dose delivery is planned to be less than 5 minutes, with robust automatic MR-MR segmentation techniques. With the time added for treatment delivery, the total time should in all cases be less than 20 minutes.

The registration between MR and CT images for target delineation purposes in a CT-based workflow is an often overlooked source of uncertainty. This uncertainty has been reported to be on the order of 2 mm (22), which is a lot for an error with systematic effects throughout the entire treatment. In the MR-only workflow, these systematic errors will be avoided. The total setup margin, including all uncertainties in the complete setup chain, will be further analyzed as part of this project.

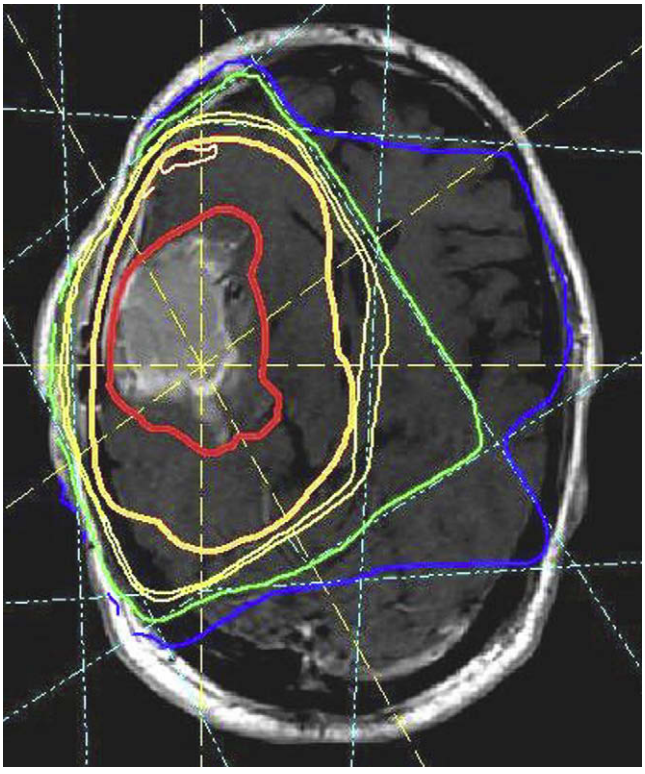

Fig. 6. Dose distribution visualized on top of MR images. GTV = thick red line; PTV = thick yellow line; thin lines illustrate the isodose levels.

The standard radiofrequency coils in the MR scanner have been developed for diagnostic purposes and are not always compatible with the radiotherapy fixations. The problem is most pronounced in the head-neck region. This incompatability has resulted in extensive use of flex coils mounted on custom-made support devices. Typical demands are that fixation devices should fit within the coils and that surface coils should not deform the patient. To achieve this, the distance to the coils will typically be larger than those for diagnostic applications. Here we see a large potential for improvement.

Generation of ''x-ray-like DRRs'' based on MR images will be required if the patient alignment at treatment delivery must be verified by 2D x-ray methods. Manual segmentation of bone for DRR generation in the pelvic region has been demonstrated in a feasibility study (17). However, for real daily clinical use, more-advanced bone enhancing MR sequences, as well as automatic segmentation of bone and air, must be developed. Computer-assisted segmentation methods based on bone enhancing pulse sequences applied for surgical purposes have been demonstrated by Hoad *et al* (23).The principle of using ultra-short echo time imaging to enhance bone visualization has been described by Robson *et al* (19).

The out-of-target dose given by a MV cone beam optimized for image registration at patient alignment varies between 5 and 15 cGy for a single 3D sequence (24). kV cone beam CT imaging can be delivered with an added out-of-target dose of approximately 2% of the target dose (25). With respect to the actual tumor treatment, this dose can be accounted for by adding it to the treatment plan, and for early side effects, this contribution can generally be neglected. However, late side effects like secondary cancers must also be considered when patients with long life expectancy are treated. This is especially important when advanced efforts like using particle therapy are applied with the intention to reduce the out-of-target dose (26). In these cases, repeated imaging would significantly reduce the advantages of these efforts. No-dose (MR) is therefore preferred at frequent setup imaging.

Since organ delineation is one of the most time-consuming procedures in radiotherapy, there is an urgent need for the development of autosegmentation tools that can be adapted to different imaging modalities and tissue characteristics. Pasquier *et al*. (27) has demonstrated that autosegmentation with T_1 and T_2 turbo spin echo MR images for prostate and healthy tissue delineation. A deformable organ model method was demonstrated to give reliable results for the prostate, and due to the soft tissue contrast characteristics in the images, the seeded region growing method was shown to give reliable results for both rectum and bladder.

Efficient biological imaging for both the initial treatment planning and the individual adoption during therapy will be easily facilitated in this workflow model due to the close connection between the treatment and the imaging units. A large number of publications have reported positive correlations between imaging of biological parameters and clinical outcome. However, these studies are generally performed with small groups of patients, in cases where more clinical experience is needed to actually obtain clinical evidence for these novel methods. The concept of integrated MR in the radiotherapy procedure will easily facilitate both the initial research needed and the future clinical implementation of biological adaptive radiotherapy.

CONCLUSIONS

MR is highly sensitive to macroscopic variation in tissue histology, and based on current experience, it can be concluded that MR-only treatment planning and virtual simulation is in many cases feasible without introducing significant artifacts in dose to or geometry of the patient. Due to the improved imaging characteristics of MR and by avoiding errors in the patient image geometry and the resulting dose distribution, an overall improvement in geometrical precision is expected.

The potential to develop the highly needed segmentation tools for tumor and healthy tissue will also be significantly enhanced through the general use of MR imaging instead of CT. However, due mainly to the better bone imaging of CT, coregistered CT/MR images will still be regarded as a complementary procedure until acceptable bone imaging methods have been developed for MR. It is, thus, acknowledged that MR imaging and segmentation of bone needs to be further developed. Repeated MR localization of soft tissue tumors at treatment setup can be efficiently performed, thus avoiding invasive procedures of implanted markers.

The logistics and infrastructure suggested here will significantly reduce the amount of workload and redundant imaging. At the same time, future implementation of biological imaging by an integrated MR and potentially by the addition of PET will be simplified.

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