Image-guided and adaptive radiation therapy with 3D ultrasound imaging

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SOCIETAL IMPACT AND VALORIZATION
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Because the topic of this thesis is already very clinically oriented, most of the valorisation is already mentioned in the discussion, but is briefly highlighted here in two and a half pages.

During the last six years we had the opportunity to use an already commercially available 3D ultrasound (US) image-guided radiotherapy (IGRT) device. We have put it through some tests and studied multiple applications among which are some new opportunities. This resulted in better understanding of the system, leading to some guidelines to prevent mistakes; a clinical workflow for the new application in the upper abdomen; and added value to the daily acquired images.

Besides the work in this thesis, another PhD thesis of Davide Fontanarosa on the speed of sound correction in US imaging was conducted in the same research group. The collaborations on that topic resulted in multiple papers and a correction method to diminish the aberrations due to differences in speed of sound in US imaging.

**CLINICAL AND SOCIETAL RELEVANCE**

**US image-guided radiotherapy: Where are we now and how did we contribute.**

Our research was useful for the radiotherapy community and for cancer patients.

We tested the robustness and made people aware of the critical issues in usage of this system. We proved the usability of the 3D US IGRT intramodality device and made it safer with some guidelines on the intermodality registration stage.

Furthermore, we tested the system for use in the clinic with prostate and liver patients. Even though the results were positive, we did not implement it into the clinic due to practical reasons. (So our own patients did not benefit directly from this research yet.)

In current practise, prostate patient get four small metal markers inserted in their prostate. This is done with large needles transrectal or transperineal a week prior to the CT-imaging for patient planning, resulting in an increased infection risk and a week delay for the start of treatment.

We have compared the current practise with the use of the less invasive US procedure, and we have demonstrated US has comparable accuracy. The US workflow does require more practice, but it might be a desired alternative for patients who would like a less invasive procedure.

For liver patient, even more practice and experience is required, but the current practice is in need of improvements. Right now there are two main solutions to position the liver patients for their radiotherapy treatment. One of them is like with prostate, insertion of metal markers. But besides the complications already described for prostate, in liver you also have the risk of tumour spill, which means that there is a risk that you spread around tumour cells, which can result in new tumours around the track of the needle. Therefore, in our clinic, the current practise is the less invasive alternative without markers. In this case the patient will be positioned based on their bone positions, or if the cone
beam CT image quality is good enough, based on soft tissue imaging around the liver. Unfortunately, the soft tissue contrast in the cone beam imaging devises currently in the treatment rooms is still relatively poor. This means that we cannot precisely/accurately visualize the tumour position. To compensate for this, wider safety margins are added to the target. With the US procedure, the imaging contrast is much better, leading to a more precise/accurate visualisation of the target, potentially resulting in smaller safety margins and better sparing of the healthy tissue.

For patients at our clinic this could have led to the introduction of a less invasive application of IGRT for prostate and a more precise/accurate treatment for liver cancer patients, but there is room for improvement in the US IGRT technique which might make it more attractive and hopefully will lead to clinical introduction in the future.

In the future, our clinic wants to get the patient more involved in the treatment decision, and I think that when prostate patients would be able to choose between US of metal markers, a lot will choose US. And I guess the same will be true for liver patient if they get the choice between US (even with all its peripheral equipment like active breathing control) or the current practice.

**Where do we want to go, and what did we do to make that happen**

For the small but growing number of US IGRT users our research provided a positive sound in the field that it deserves a (second) chance to prove its capabilities. Furthermore we managed to build a US IGRT platform/workshop to share and present ideas for current and future research. And the interest of a new major commercial partner who recently became interested in this topic was gained. With this new network we believe much more constructive partnerships and collaborations can be reached to make a move forward.

The radiotherapy field is more and more heading towards adaptive radiotherapy (ART) in which the radiation plan is adapted to the current anatomy of the day for each individual patient. With our research we showed that also US IGRT has capabilities that could be used for ART.

During the work with the system and the implementation of the technique, more and more topics and possible innovations became of interest for future research, but were not directly part of this thesis.

One example would be making the process less user dependent with more automation with for instance auto-contouring and non-handheld probes. Another application would be intrafraction motion monitoring, which helps us to image the irradiated structures, which would be a great step forward. Also improved contrast (e.g. contrast enhanced ultrasound) and functional imaging for targeting and treatment evaluation would benefit the field. So there is still a lot that can be done and our research group is continuing in helping to find the optimal solution.

**How will we get there**

The base and support for US IGRT is still rather small and US imaging is not seen as trendy. But innovating medical devices does not always require the development of new techniques. Sometimes the adoption and adaptation of old(er) techniques in new workflows is
the innovation. Because US is an non-invasive technique maybe we should involve the patients more to convince the doctors. By making the patients aware of the different ‘flavours’ in the positioning techniques for radiotherapy treatment this might give them a preference for different treatment institutes. For instance through patient group websites this awareness could be spread.

But more importantly, with automated US probes, most of the US workflow issues that held back the usability so far will go away, and will no longer stand in the way of the benefits of a non-ionizing imaging technique. If we really are heading towards daily imaging before and possibly even during treatment, current imaging techniques increase the radiation burden on the healthy tissue. With the use of US IGRT, this damage to the healthy tissue can be avoided.

**ECONOMICAL RELEVANCE**

Because of the interest in tracking the target motion during treatment, there is also a need for phantoms to perform quality assurance and quality control. Our group has been working on a design for a 4D phantom that is currently under evaluation for patent submission together with a medical industry partner.