MRI Guided Radiotherapy: a direct hit

Inaugural lecture of professor Bas Raaymakers
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Introduction and rationale

Mijnheer de Rector Magnificus,
Geachte collegas, dear colleagues,
Beste familie en vrienden,
Waarde toehoorders!

Wow and welcome, again. Well, MRI guided radiotherapy: a direct hit.

Clearly I am referring to our new radiotherapy system, the MRI linac, a linear accelerator, in short a linac, with integrated 1.5T MRI functionality for imaging. We started working on this in 1999, so time wise, it is not exactly a very direct hit but in many other ways, it is.

The MRI linac originates from the desire to have a radiotherapy system that can detect and visualize any geometrical change in the patient and adapt the radiotherapy dose accordingly, in real-time. This way, we can directly hit the tumor and always minimize the burden to the surrounding structures.

But why did we go through all the hassle to build this new system? For people outside the radiotherapy field, for instance students entering our department for a master project, this whole project can be a rather surprising exercise. Nowadays, people are connected to the rest of the world, information is almost freely available, your mobile phone can give you directions to anywhere in a split second, and you know what others are doing where. The expectation is that for the rather dangerous and critical process of hitting a tumor with a beam of ionizing radiation there is similar information available, full 3D visualization and precise information on the location and shape of the tumor throughout the entire process.

But in reality, and now I am quoting my esteemed colleague professor Oelfke from the Institute of Cancer Research in London, in radiotherapy "we are trying to hit an invisible target with an invisible beam". Moreover, radiotherapy is typically delivered fractionated, so over a series of days to weeks. And every fraction, we try to hit the target and as little healthy tissue as possible with our invisible beam. But we know that there are anatomical changes from day to day: patients lie slightly different on the table, there might be weight loss or changes in bowel filling, or the tumor may have responded to the radiation. And there are variations during a single fraction, for instance bowel motion or respiratory motion, while this breathing pattern can also be irregular.

Right now, all of this is invisible to us during radiation delivery. To account for such uncertainties and also for undetected changes in the anatomy, a safety margin around the tumor is included as target. This way the tumor coverage is
guaranteed, but at the price of frequent and unwanted irradiation of large volumes of healthy tissues in this margin.

But, let's not panic, of course, this is recognized as a problem and much effort has been, and is being put into estimating the tumor location during delivery in order to minimize the margins and thus healthy tissue involvement. X-ray photos or conebeam CT imaging of the patient on the treatment table can be used to reveal the tumor or reliable surrogate landmarks. And if you have representative anatomical landmarks or fiducials and not too much irregular motion, the tumor position can be estimated accurately and margins will be small enough to deliver the required dose to the tumor with acceptable toxicity. For instance peripheral lung tumors can be detected using conebeam CT, or the prostate gland can be detected by using fiducial markers, both just prior to radiation. These data are then used for high precision and highly effective radiotherapy.

We want this type of high precision, highly effective radiotherapy for any tumor and we do not want to estimate the tumor position and the surrounding. We want to see it, during delivery and we want the possibility to act if things change. And MRI can offer all of this.

Soft-tissue structures can be visualized, in this case the rectum and its surroundings and also motion can be detected and quantified as shown here for the liver.

This is in a nutshell the goal of the MRI linac: bring sight to the radiation oncologist and offer the ability to change the treatment based on what you see.
Whether we need this for all tumor sites and how much clinical gain we will have has to be determined in clinical studies. I think that for many tumor sites, future radiation oncologists will shiver when they think back at the times when there was no direct sight during delivery. By then, one will have to defend why sight is not important rather than arguing about the need for it.

**The evolution of the MRI linac**

We have, in close collaboration with Elekta and Philips, progressed on the development of the MRI linac quite well and also quite fast if I think about it. Time flies when you are having fun. And of course we are working for the good cause, but it really helps that it is great fun and very rewarding to assemble big pieces of high tech machinery to achieve a high precision medical device. The very first prototype is shown here.

It shows a static linac next to the MRI, you can appreciate the non-clinical looks of it. This was the proof of concept, diagnostic quality 1.5 T MR imaging during radiation delivery was shown feasible, on a porkchop. This system was upgraded as shown here.
This system allowed us to proof that a rotating gantry and a multi-leaf collimator could be added without detrimental effects and that intensity modulated radiation therapy during MRI guidance became possible as well as MRI based gating and tracking of the radiation beam. The latest step is the development of a clinical prototype, shown here.

This is how the clinical prototype looks like, with and without covers, it is getting pretty clinical looks. Elekta is shipping the first clinical prototypes as we speak. It is quite exciting, the MRI linac is really going to happen! So the MRI linac technology is here and now what?

I know I am biased, but in my mind it will have a large impact. And we are working towards having a great impact. It is not just a new machine for the radiotherapy clinic. From a technological point of view, new application fields such as MRI, image processing, treatment planning, on-line quality assurance, all
needs to be explored or re-invented to fully exploit the possibilities of real-time imaging during radiation delivery.

But things will change for the clinical practice too. When the radiation oncologist can directly see what is being hit by the radiation beam, it becomes very much like a surgical procedure, but then, without a knife, radiosurgery if you will. This demands new workflows and operator responsibilities, dose prescription and fractionation schemes. Also the relation to other oncological treatment modalities needs to be addressed and will very likely be re-defined.

Together this should lead to the most important impact, on patient care. For instance by offering an alternative for partial nephrectomy for kidney cancer patients. We want to offer an out-patient, totally non-invasive, ablative treatment with higher curation rates and less toxicity than currently done with surgery.

**Technological impact of the MRI linac**

Let's start at the technological impact for the radiotherapy field.

**MRI for MRI guided radiotherapy**

What we need first of all is MR imaging dedicated for radiotherapy. MRI is very versatile and wide spread in radiology. However for radiotherapy delineation purposes, let alone for on-line radiotherapy treatment guidance, we have specific, different requirements.

We need fast, volumetric data, for initializing the treatment and we need 4D MRI to track any geometrical change in the patient during treatment. To account for inevitable latencies, also modeling and motion prediction will be part of the research. Also we need to be able to calculate the dose distribution based on these MRI data. And for evaluating or predicting treatment response, we need to understand functional parameters. Because MRI is very versatile, these requirements can probably be met or at least be approximated, in the past many artifacts have been turned into useful contrasts.

But before this is standard practice, this is a research arena by itself and demands MRI physicists at, or working for, the radiotherapy department. We do cherish our MRI physicists, and so should you because there will be many at your department! (But they are nice!)
This is an example of what can be done, a 4D trajectory of the pancreas, so a trace in 3 dimensions as function of time, established via a combination of modeling and fast MRI.
Image interpretation for MRI guided Radiotherapy

Partly related to that is the image processing. Updated MRI data is one thing, interpretation of these repeated data is a separate challenge. Currently, the starting point in radiotherapy is that physicians manually interpret the data, that is, delineate all relevant structures. For the MRI linac we need an automated approach as daily and ultimately real-time, manual delineation is not realistic.

Identifying the tumor volume on MRI is a research topic on its own. It requires an interplay with the MRI physicists (again) to optimize the contrasts for relevant landmarks and functional parameters, together with pathology to determine a ground truth. Also, detailed geometric dose response data can contribute to the target identification, something the MRI linac can provide, as I will discuss later.

But for the use case of the MRI linac, the challenge is different, in my mind easier. In the pre-treatment phase, physicians have approved all relevant structures, either generated by hand or automatically. So we have prior knowledge and “only” need to propagate this onto the latest MRI. This automatic propagation needs to be validated against reliable and consistent manual delineations. These will come from ongoing and future consensus guidelines and delineation protocols.

As such MRI guided radiotherapy will provide a wealth of benchmark data and we should use this opportunity to progress the automated image processing and registration algorithms to extend the interest and involvement of the image processing community. I think this is especially true for dedicated tasks such as image registration and contour propagation on an intra-patient basis. An on-going example is the adaptive atlas based image registration of Elekta to propagate the initial delineation data to a new MRI of the same patient. This needs to be extended to arbitrary structures and also to the use of additional, multiple, repeated data of a patient for further optimization of subsequent contour propagations.

Another improvement to use the prior knowledge as effective as possible is to tailor the image registration algorithm and the MR imaging to each other. In collaboration with the group of professor Moonen, the synergy with MRI guided High Intensity Ultrasound was used to demonstrate this. An optical flow method and fast MRI were jointly optimized to facilitate robust, real-time tracking in 3D as shown here.
Pancreatic motion is not tracked via modeling as shown before, but in this is truly in real-time.

**Automated treatment planning**

When we have a continuous update of the patient anatomy, we have the responsibility to do something with it. Instead of using a single treatment plan for the entire treatment we should adapt to these changes. We want to have a dose distribution tailored to the latest state of the anatomy instead of estimating the position and use a large "better-safe-than-sorry" volume around the tumor as a target. The more frequent the adaptations are, the higher the need for automatic treatment planning becomes. The real-time feed-back of the MRI linac will boost the development of real-time, automatic treatment planning.

In the group of professor Heijmen from the ErasmusMC in Rotterdam, Sebastiaan Breedveld already showed that full automated treatment planning is clinically feasible while in the group of professor Oelfke in London, Peter Ziegenhein demonstrated that real-time, interactive plan adaptation is possible. These technologies are needed to enable real-time adaptation to anatomical changes. Specifically for the MRI linac, we have developed automated daily and intra-fraction plan adaptation strategies.

Automated treatment planning can also generate an entire set of treatment plans and offer the physician a choice of different trade offs for a certain patient. For the MRI linac I think the main aim of automation is speeding up the planning process in order to accommodate anatomical changes instead of offering a choice of plans for each point in time.

**Online Quality Assurance**
Then, to guarantee the safety of highly automated, often adapted radiotherapy treatments new, on-line quality assurance, in short QA, procedures are required. To get there, we start with the existing QA procedures for the MRI side and for the radiotherapy side of the MRI linac, as used in the regular diagnostic and radiotherapy clinic.

However, already here a new field of research is opened since the dose with the MRI linac is delivered in the presence of a magnetic field. The dose distribution is different, which demands dedicated new procedures for verification, but also radiation detectors are affected by the magnetic field and need new calibration and operation protocols. All existing radiation quality assurance procedures need to be revisited for the MRI linac.

As the project progressed, industry recognized this new opportunity and currently we are evaluating new detectors and phantoms from PTW, IBA, Sun Nuclear, Scandidos, CIRS, Modus Medical, Philips and of course Elekta, many thanks for this support. Also the national metrology laboratories of the U.K., NPL and especially of the Netherlands, VSL are involved to set-up new traceable absolute radiation dosimetry standards for the presence of magnetic fields. In addition tests are required to evaluate all aspects related to the hybrid character of the system, which basically boils down to assessing the MRI based feed-back loop for treatment control.

So far, this is all about checking if the machine performs as it should, the classical QA if you will. To check the actual MRI linac treatment and the on-line plan adaptations, automated, on-line, quality assurance on the procedure rather than on the machine performance will be necessary. Initially this will rely on manual assessment, but that should lead to class solutions for the workflow for which action levels are determined and can be verified off-line.

**MRI based dose reconstruction**

Something that will contribute to on-line QA is MRI based dose reconstruction. The MRI linac provides volumetric data including the evolution in time, while also the radiation output from the linac is time stamped. For on-line machine QA, these recorded machine parameters can be compared with the planned parameters. And by combining the MRI and machine parameters, the evolution of the dose in a dynamic anatomy can be followed. For checking the treatment decisions, the reconstructed dose can be benchmarked against the planned or reference dose distribution using an independent dose engine.

At the same time MRI based dose reconstruction will reveal the response logic for radiotherapy. Tumor recurrences can be correlated with the true dose distributions so biological parameters can be better spatially correlated with the dose response. This facilitates better understanding of the underlying biology and its relation to the physical dose distribution, something that can be used for the earlier mentioned tumor identification.

**Impact of the MRI linac on the radiotherapy clinic**
Now let’s shift gears to the clinical impact.

**Clinical impact**

When looking at the clinical impact of the MRI linac, the overall aim is quite simple, radiotherapy with more cure and less toxicity, not only for the currently treated tumor sites, but also for tumors which can not be satisfactorily treated with the current equipment such as kidney tumors.

The technological work is all focused to facilitate on-line, MRI based plan adaptation, or as summarized nicely by another esteemed colleague, professor Pignol from Rotterdam, to facilitate “You see it, you zap it!”. And on a pork chop this is easily done and demonstrated, but to do this clinically, the physicians need to re-invent existing, or adopt new treatment paradigms and built up new clinical experience for these approaches. To achieve this, the radiotherapy clinic will change and also, we need large scale collaborations to let this land in the radiotherapy community.

**The Atlantic consortium**

This was also recognized by Elekta, and therefore they launched the Atlantic consortium.

The MD Anderson Cancer Center in Houston, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital in Amsterdam, Sunnybrook Health Sciences Centre in Toronto, The Froedtert & Medical College of Wisconsin in Milwaukee, the Institute of Cancer Research with the Royal Marsden NHS Foundation Trust in London, the Christie NHS Foundation Trust in Manchester and of course our University Medical Center in Utrecht all get similar copies of the MRI linac as shown earlier and together with Philips and Elekta they will join forces to clinically introduce this system in a coordinated fashion.
This will not only improve and accelerate technical developments but also align clinical protocols and data collection for evaluation. In this context I want to thank professor van Vulpen and Linda Kerkmeijer for their great job and enthusiasm in aligning, exchanging and chairing these clinical activities, and I can add that I speak on behalf of many within the consortium. I am very happy and proud on this consortium, and it is reassuring to have such an assembly of brains working towards the same goal.

Competing MRI linac systems

But the collaboration should not be limited to the consortium. Others have adopted this idea of MRI guided radiotherapy too and are also pushing developments forward. In Sydney, professor Keall is building a hybrid 1.0T MRI linac system, in Edmonton, professor Fallone has an operational prototype 0.5T MRI linac and the Viewray company has already installed multiple 0.3T MRI Cobalt radiotherapy systems and have treated patients with it.

Of course, I know that we have the very best system and as the founding institution, we would have liked to be the first ones treating patients but at the same time it is good to see the idea is picked up and implemented in various ways. Similar to the consortium, there is inevitably some competition, but we should focus on the common ground and team up as MRI guided radiotherapy guys and girls to the rest of the world. Then, together with the consortium we will convince the community of the added value of MRI guided Radiotherapy.

Clinical introduction via clinical trials

For the MRI linac there is already a shortlist of nine tumor sites for the initial clinical trials, the exact order of introduction is still under debate. But obviously we will start safe and simple and only gradually work towards implementing real-time MRI based plan adaptations for arbitrary tumors. The first-in-man treatments are decided on and this tumor site will be spinal bone metastases.

For these first-in-man treatments, all the technology has to come together in order to prove that this new system can indeed bring the new paradigm of on-line MRI guided plan adaptations safely into clinical practice. The endpoint of this very first trial is not clinical benefit but demonstrating technical feasibility and safety of on-line MRI based plan adaptation and MRI based localization.

The good thing about the bony target structure is that the on-board portal imager can be used as an independent verification on the MRI localization. Also the on-line quality assurance can be brought into clinical practice, MRI based dose reconstruction can be validated and the independent machine parameter check can be verified, again using the portal imager.

After this is successfully done, the real exciting, and by times stressful period will start. Different additional tumor sites will be brought to the MRI linac in joint, consortium wide, trials to demonstrate the clinical value of the MRI linac. Again, increasingly sophisticated adaptation strategies will be rolled out over time. I
have great confidence in the consortium for doing this with the appropriate consideration, and I am convinced that the results will be rewarding and something to celebrate together.

Commercial introduction of the MRI linac

The Viewray system is already on the market right now, Elekta will start selling in 2017 and deliver in 2018. And given the current, and growing, interest in MRI guided radiotherapy, it looks like the growth of install base will be limited by production capacity rather than by customers.

Still, the coming years not too many clinical results will be available, and, many institutions will have to learn MRI and learn how to exploit it for radiotherapy, for instance for MRI simulation, MRI based treatment planning and MRI based response assessment. There need to be more MRI access from the radiotherapy departments either via good collaboration with radiology or by buying one.

It would be wise of the vendors to supply virtual MRI radiotherapy functionality on these diagnostic MRI systems, so dry-run MRI guided radiotherapy can be performed. This is a necessity for treatment preparation for the MRI linac and it would facilitate the learning curve of radiotherapy departments ahead of having a real MRI radiotherapy system. It is an additional argument to bring more MRI systems to radiotherapy and it is a new market opportunity by itself.

MRI guided proton therapy

MRI guidance will improve external beam radiotherapy, but this is equally true for other modalities such as proton therapy. Often, the MRI linac and proton therapy are seen as antagonists. This debate is easily polarized which only erodes the position of radiotherapy in oncology. Whereas both try to achieve the same goal, more dose to the tumor, so more cure, with less dose to the surroundings, so less toxicity. The MRI linac is closing in on this goal by providing sight for a more direct hit, and in proton therapy the beam can stop inside the patient.

A seemingly obvious improvement is combining these two and realize MRI guided proton therapy. Scientifically, we should absolutely go for a hybrid MRI proton therapy machine. It provides a new research arena, will challenge the existing solutions and by doing so improve these. Clinically, it remains to be seen if the technical hurdles can be solved adequately.

In Utrecht we will try to quantify how MRI guidance for radiotherapy and proton therapy relates in order to put data on the table when making the clinical assessment or strategic decisions for X-ray or proton therapy, respectively with or without MRI guidance. Also this will provide the rationale for working towards a prototype MRI proton therapy system; no matter how cool a prototype would be, we need more arguments to involve other parties and justify the investments.
We have started this exercise for pediatric patients and in this context I am very happy with the collaboration with the "Prinses Maxima Centrum" for pediatric oncology and I am convinced that these MRI guided proton therapy activities will contribute to their international research ambition too.

*Other MRI guided oncological treatment modalities*

Yet another ionizing treatment modality is brachytherapy. MRI guided brachytherapy is already clinical standard for cervical cancer, the geometrical control of the dose distribution led to nearly 100% local control with fewer toxicity. MRI compatible implantation techniques are under development and will challenge the other radiotherapy modalities.

And then there are also non-ionizing modalities, such as MRI guided HIFU, High Intensity Focused Ultrasound, where tissue is thermally ablated under MRI guidance. In Utrecht professor van den Bosch and professor Moonen are optimizing the technology while also exploring these interventional radiology treatments.

*Multi-modality oncological treatments*

Now, in radiotherapy we are used to optimizing a treatment to maximize the dose to the tumor and minimize the dose to the surroundings. But typically this is done for a single modality whereas multi-modality treatments might be much more efficient.

If the tumor is visible and accessible for a brachytherapy needle or the HIFU focus, the integral dose will be much lower than any external radiotherapy modality can ever achieve. At the same time, there are always uncertainties in the process and external beam radiotherapy has all the clinical experience there and has a therapeutic window of discriminating tumorous and healthy tissues via fractionation.

*Center of Image Sciences in Utrecht*

We should optimize all these modalities individually and at the same time investigate the balance and identify the optimal multi modality treatment. And that brings me to something close to my heart: the Center of Image Sciences here in Utrecht. Within this collaboration of radiology, nuclear medicine, radiotherapy and image sciences we have expertise ranging from fundamental technology development to clinical trials and routine clinical practice. It is a real powerhouse with close to 100 PhD students addressing topics related to MRI and oncology.

Sometimes I get the question why I never left Utrecht, and this is why, this is simply the best place on earth to develop technology and translate it into the clinic! I would like to thank professor Mali and professor Lagendijk for initiating this visionary setting and the board of the UMC Utrecht for having the courage to facilitate this. This setting allows the optimization of the individual modalities.
and exploitation of the synergy of MRI guidance. Within the Center of Image Sciences we will clinically introduce the various techniques, and compare clinical results but also cost effectiveness and, investigate multi-modality approaches.

**Workflow for MRI linac and conventional linac treatments**

This multi-modality approach will already start at the radiotherapy department by using both the MRI linac and a conventional linac for a single patient. A single patient can undergo regular radiotherapy for treating these parts of the target that are geometrically uncertain or remain invisible, think for instance of microscopic tumor infiltrations, while parts of the tumor that are visible can be boosted, potentially even ablated with the MRI linac. This will bring dose painting to a new level.

Executing the part on the conventional machine is daily practice already, the MRI linac will demand a different workflow and staffing. These will typically be fewer sessions, so hypo-fractionated treatments, and are interactive, much like brachytherapy, interventional radiology and surgery. The responsibilities for treating will shift from the pre-treatment phase towards the control room. And the emphasis of quality assurance will shift from technical performance towards the clinical decisions. Initially, this will be done manually. By professionals, so the physicians but also parts of the process such as contour or plan evaluation will be delegated to dedicated therapists. This should yield the input for the earlier mentioned class solutions on workflow.

**Relation Radiotherapy and Radiology**

If you take this one step further, you come to one-stop-shop treatments, where also the diagnosis is done or confirmed. Then MRI linac treatments basically are interventional radiology, providing another reason for radiology and radiotherapy to team up.

Once again, this is why Utrecht is such a great place to work, this is already taking place within our Center of Image Sciences. Our head of radiotherapy, professor van Vulpen is teaming up with the head of radiology, professor van den Bosch to investigate and build this clinical infrastructure and progress image guided oncology.

**Wrap up and acknowledgements**

Let me try to wrap up.

The MRI linac project started in 1999, while my professional journey in UMC Utrecht started already in 1995. During this period I became indebted to very many people for their support and contributions, simply and unfortunately too many to mention individually. I can only hope that I can return at least part of that support sooner or later. Also I hope that for now you will accept this little bow as a token of massive appreciation.
Of course I will make a few exceptions. First of all to the PhD students that dared to give their life to science under my supervision, thank you, you make the things progress!

I also would like to show this photograph from 2008. The occasion was a STW, Dutch Technology Foundation, user-committee meeting. I would like to thank STW for their support in the critical start-up phase in this project. You see here Kevin Brown from Elekta, Johan Overweg from Philips and Jan Lagendijk, Jan Kok and myself from UMC Utrecht. This collaboration lasted all this time and brought us to where we are today.

Kevin, thank you personally for your friendship, long term involvement, right from the start of the project. You faithfully represent the core values of Elekta: long-term relationships, trust and responsibility, responsiveness (“very interesting!”) and creativity. Also I am asking for your responsibility in this case to accept this thank you on behalf of Elekta as a whole and to bring across my thanks to all the Elekta people involved!

Johan, without you there would not have been a MRI linac right now, you are one of the most knowledgeable people in the field of MRI hardware, and any MRI related argument could be solved by saying that it was discussed with you. Of course, I would like to extend this thank you to all the Philips people involved.

Jan Kok, it has been said before, your contribution cannot be exaggerated, you built the first prototype from semi-legal Chinese documentation and ever since kept the system alive.

Then Jan Lagendijk, my supervisor, my mentor, partner in crime and what have you. We shared a lot, including a king size bed in Puerto Rico. Your endless optimism and directness are legendary. You are a great example and role model for me. And for those that might find that a bad idea, do not worry, Jan cannot be equaled.
We started as a little party on a quest, and look what we found, a ring!

It did have this strange attraction and great power, but in this story line, we did not need to destroy it but we could celebrate it as a critical milestone on the way to real-time MRI guided radiotherapy.

Natuurlijk, ben ik ook buiten mijn professionele leven vele mensen dankbaar voor hun bijdragen en hun liefde en waar nodig een reflectie. Gelukkig ook hier weer te veel op op te noemen, ik kan alleen maar hopen dat veel mensen iets van hun bijdrage terug zien in mijn gedrag.

Een paar mensen die een grote impact hebben gehad wil ik graag met name noemen. Ruud Diterwich en Erik de Feijter, met Ruud kan alles in twijfel getrokken worden, en met Erik lossen we alles met de grootste stelligheid op, ik hoop daar nog lang mee door te gaan.

En dan mijn vader, helaas heeft hij alleen de aanloop van dit project meegemaakt, maar ik vind het mooi dat zijn vaak gebruikte "Weet je wat we doen, we zien wel!" feitelijk ook het motto van de MRI linac is, zo is hij er toch ook een beetje bij.

Natuurlijk mijn moeder, onvoorwaardelijke liefde en mee-levend tot op het nerveuze aan toe. Mam, elke keer als ik doorzettingsvermogen nodig heb, ben jij mijn voorbeeld.

Mijn zusje en broertje, Olga en Maarten. Olga laat me zien dat het inrichten van je leven je eigen keuze is en dat van klein geluk, groot geluk komt. Maarten laat me zien hoe je ambitie combineert met het genieten van klein en groot geluk.

En dan, mijn schatjes, Pepijn, Jitske en Tijler, een betere en een leukere spiegel dan jullie kan ik niet hebben. Jullie zijn mijn eigen consortium en powerhouse, alle energie die ik in jullie stop komt niet per se gecoördineerd, maar altijd in veelvoud terug.

Niet, ik ben trots op je, blij met je, samen zijn we hier gekomen en dat belooft veel goeds voor de toekomst. Jij bent natuurlijk mijn enige echte "direct hit"!
As a final remark I would like to mention that one should not shoot the messenger, but also, one should not praise the messenger. I have been very fortunate to have been working and still am working with so many different people, so many bright people. I am proud on how far we got, and I am absolutely thrilled when I visualize where this will go now more and more people get involved. An audience like today or the last two days is encouraging and makes me feel humble at the same time. I am very much looking forward to the collaboration with many of you and together make MRI guided radiotherapy a great hit.

It will be much like discussed by this little happy fellow: "Everything familiar has disappeared!", "A fresh, clean start!", "It’s a magical world", "Let’s go exploring!". And to this I can only add: "Hey ho, let’s go!"

Ik heb gezegd.