MRIdian 50/5

Summer 2020

GenesisCare

"Sometimes you think: wouldn't it be better if we had better technology to overcome this difficulty"

Dr Veni Ezhil
Clinical Oncologist

Contents

Introducing the UK's first MRIdian MR linac

GenesisCare is an independent provider of advanced and innovative radiotherapy and cancer therapies. We operate specialist oncology centres across the UK, Australia, Spain and now the USA, and work with leading oncologists and surgeons to design and deliver cancer care that improves life outcomes for our patients.

As a successful global company, we have a responsibility to share world-class expertise and are fortunate enough to be able to invest early in new evidence-based treatments and care that will make a difference. MRIdian is one such innovation.

MRI-guided radiotherapy has been described as a new paradigm in radiation oncology. It is a technology that has been adopted by some of the world's leading teaching and public hospitals. In 2019, GenesisCare installed a MRIdian MR linac at its centre in Oxford and became part of the global radiotherapy community that is driving the adoption of this game-changing treatment. This was the first MRIdian in the UK.

The MRIdian MR linac is one of the most advanced forms of radiation therapy, demanding a high level of clinician input, a skilled team, a robust workflow and a completely new way of working.

GenesisCare overcame these challenges and we were able to set up a service in six months and then treat our first 50 patients during the next five. In that time the benefits to patients have been even greater than any of us imagined.

MRIdian 50/5 chronicles our experience. We want to share what we've learned so that other centres can replicate this service with the same efficiency and positive outcome. MRI-guided radiotherapy will play a major role in cancer care in the next five to ten years and will be adopted by many more healthcare organisations.

Why MRI-guided radiotherapy

We hit the target every time

Stereotactic ablative radiotherapy (SABR) is a technique that is growing in its impact in the UK. Magnetic resonance image-guided radiotherapy, or MRIgRT, is the next step in the evolution of this treatment. It is delivered using an MR linac, which combines an MRI scanner with a linear accelerator. Using MRI instead of CT enables high-quality, continuous soft tissue visualisation for patient position, set-up and verification which in turn allows for reduced uncertainty margins to be used during treatment planning.

The MR linac delivers two main features: the ability to perform daily adaptive treatment planning and real-time, on-table guidance to allow for daily changes in the position of internal structures or organs at risk (OARs). An additional feature of the MRIdian MR linac is automatic gating so that the beam switches off when the target moves out of the gating boundary. This makes it possible to monitor intrafraction motion caused by breathing or organ-filling.

"It is such a well-designed system that the whole is more than the sum of its parts. We can achieve something clinically that we would have struggled to achieve on any other machine. It's a tool for delivering the best quality SABR possible"

Dr James Good

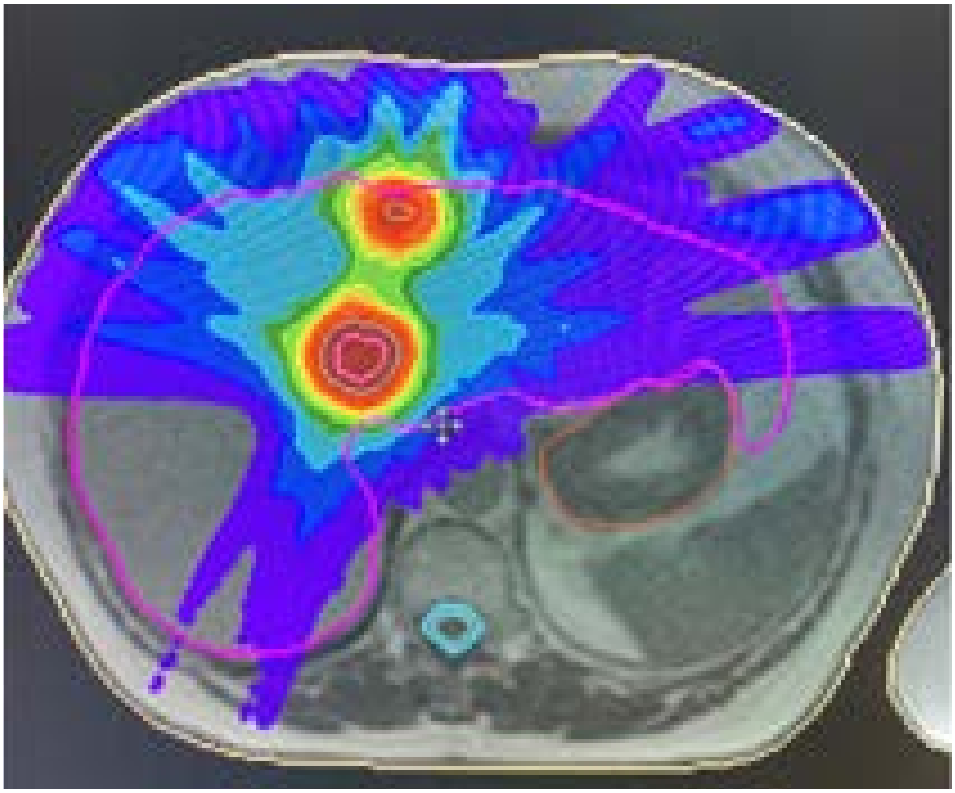


Fig 1: Multiple liver metastases being treated on the MRIdian system

50 Gy in 5 fractions – with absolute precision

From a clinician's perspective

"What it's really good for is for any tumour that moves significantly with breathing or other organ motion, or where there is a critical normal structure close by."

Dr Andy Gaya

"The MRIdian gives us much more detail in terms of what we can delineate to ensure that we're treating the right area. It allows us to treat what we see on the day"

Dr Ami Sabharwal

"The ability to visualise the tumour more accurately, to follow it while it's being treated, to adapt the plan every day. MR linac is the next evolution in treatment for liver tumours and pancreatic cancer in the UK."

Dr James Good

"What is incredible when you're watching an MR linac in real time during treatment is seeing how much movement there is just during the delivery of a single fraction. Watching a piece of bowel gas pop into view is amazing; the treatment can be stopped until it moves through."

Dr Nicola Dallas

"Having worked with doctors for nearly 20 years it was fantastic to see the how the technology both stunned and surprised the clinicians. It is so rewarding to see their energy and enthusiasm for treating patients with MRIdian."

Paul Gearing
European Head of Clinical Access and Partnerships

Section one: Building a world-class service

Section one: Building a world-class service

Our team of specialists

MRIdian specialists

The introduction of MRIdian to the UK has been overseen by Specialist Reference Groups, selected by members of our Specialist Clinical Reference Groups for their expertise in urological cancers and stereotactic ablative radiotherapy (SABR). The groups work closely together in a robust forum to guide all aspects of clinical governance, patient selection, peer review, education and credentialing.

Dr James Good
Clinical Director of Stereotactic Radiotherapy, GenesisCare UK Birmingham, Oxford

Special interests: colorectal, HPB and head/neck cancers

"In my NHS Centre in Birmingham we operate one of the UK's largest liver multidisciplinary teams (MDTs) and have introduced new treatments, including SABR. MR linac is an opportunity to continue that progress. I saw its potential as the next evolution for SABR liver tumours in the UK."

Dr Philip Camilleri
Clinical Director of Urological Cancers, GenesisCare UK, Oxford

Special interests: urological cancers

"I had a taster of MR linac because I had visited ViewRay in California to see directly for myself what it could do, so I was already hooked well before I could work on the machine myself. MRI-guided radiotherapy is one of THE future directions of radiotherapy."

Dr Nicola Dallas
Clinical Oncologist Oxford, Windsor

Special interests: urological and head/neck cancers

"I was aware of the work being done at the Royal Marsden. It's an opportunity I would not ordinarily get in my NHS practice, to develop my skills and work with this new technology – and to be able to offer it to my patients."

Dr Prantik Das
Clinical Oncologist Nottingham, Oxford

Special interests: urological and lower GI cancers

"I'd known about MRI-guided radiotherapy for some time. It's the most cutting-edge breakthrough in the radiation oncology community. Getting that service in the UK and being able to treat patients here is fantastic. I was honoured to be chosen to be part of it."

"Our strength is that we are staffed by leading clinicians"

Niall McAndrew
Physics Service Development Manager – Europe

Dr Veni Ezhil
Clinical Oncologist
Guildford, Oxford

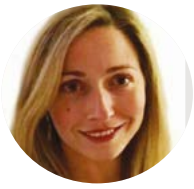
Special interests: thoracic cancers and lymphoma

"My interest has always been advanced radiotherapy and what's next. When we were commissioned to do oligometastatic disease with SABR at the Royal Surrey we were one of the few centres in the country. I'm always interested to see what can be done better with SABR, so when I had the opportunity to work on MRIdian I couldn't resist."

Dr Andy Gaya
Clinical Oncologist
London, Oxford

Special interests: upper and lower GI and Hepato-Pancreato-Biliary (HPB) cancers

"MRI-guided radiotherapy is at the cutting edge of what's currently technologically possible and I was fortunate to have been in the right place at the right time when GenesisCare were putting together a rota of oncologists to staff the machine. When we created the service, I was an NHS consultant elsewhere but over the months I have dedicated myself to treating patients on the MRIdian and other state-of-the-art treatment platforms."



Dr Carla Perna
Clinical Oncologist
Guildford, Oxford

Special interests: urological cancers

"I knew it was the most exciting development in radiotherapy for many years. It will come in slowly in the NHS, but GenesisCare were ready to start so I took the opportunity to join them. In five years' time everyone will have hypofractionated radiotherapy – this is a very safe way to do it."

Dr Ami Sabharwal
Clinical Oncologist
Oxford

Special interests: urological cancers

"I was keen to experience the game-changing technology of the MRIdian having heard about its use in other centres outside the UK. I hope my training and experience with the MRIdian at Genesiscare will place me in a good position to bring my skills back to the NHS in the near future."

Specialists/expert advisory team

MDT

Clinicians are supported by a team of expert physicists, dosimetrists and radiographers and collectively form the multidisciplinary team (MDT) that is central to the MRIdian service.

Dr Ben George
Clinical Scientist and Lead Physicist

"MRI-guided radiotherapy is the latest and greatest in radiotherapy. I've worked in research and as a clinical physicist and joined GenesisCare to be part of this - it ties all my interests together."

Adam Nash
Senior Dosimetrist-Specialist
MR planning

"I had been involved in innovative radiotherapy with the PACE trial – a large- scale research trial into SABR. Having previously planned prostate SABR, plan of the day for bladder and isotoxic treatments on the conventional linear accelerator, I was specifically recruited for this role."

Donna Hughes
Lead MR linac Radiographer

"I have experience in SABR, SRS and MRI. For me this is about wanting to be part of the next step in radiotherapy treatment and being able to combine my experience to provide the best care possible."

"The MRIdian staffing model requires a multidisciplinary team of professionals on set during treatment, including clinicians, physics, dosimetry and radiographers, all working together to achieve the best possible outcomes for patients"

Gillian Taylor, Centre Leader, Oxford

Specialists/expert advisory team

The project team

Paul Gearing
European Head of Clinical Access and Partnerships

"Our MRIdian vision started as a conversation over a coffee at Birmingham New Street Station between James Good and I. It has turned out to be the most rewarding project I have ever been a part of."

Niall McAndrew
Physics Service Development Manager – Europe

"I've had a lot of experience setting up conventional radiotherapy centres. We know that MRI holds a lot of benefits for radiotherapy, so it was exciting to be one of the first in the UK to make it available."

Gillian Taylor
Centre Leader, Oxford

"It's great to get support from the GenesisCare board for such amazing technology, we are really fortunate to be able to offer this service."

Steve Bounds
Head of Engineering – Europe

"As engineers, it's really interesting to learn something new. For me and my team MRIdian wasn't easy to learn, but everybody wanted to do it. It gave us something new to focus on."

"We're really lucky – every single member of the team is great. There's a degree of trust that has been built up across the different disciplines over the last six months. We know and understand what each other does"

Dr Philip Camilleri

Expertise from around the world

"We built this service on the shoulders of our colleagues around the world"

Dr Philip Camilleri

Acquiring the knowledge we needed to build a service from the ground up was mostly achieved with the support of the centres of excellence who were already operating a MRIdian service.

These included Carbone Cancer Center at the University of Wisconsin, one of the leading sites in the world, who have been operating a MRIdian service for over six years. Professor John Bayouth, Head of Physics, and Kate Mittauer supported during commissioning and shared their extensive knowledge and processes.

The teams also visited VU University Medical Center in Amsterdam which has two machines and is one of the three leading sites in the world.

Other sites included Acibadem Maslak Hospital in Istanbul, Heidelberg University Hospital, Henry Ford Hospital in Detroit, Miami Cancer Institute, Siteman Cancer Center in St. Louis and UCLA Medical Center in Los Angeles.

Not only did the GenesisCare clinical and installation teams visit all these sites and learn from them, we have set up lasting relationships with them for ongoing support

"The MRIdian team has had the opportunity to train with different centres around the world. This has enabled us to learn from their experience and deliver high-class care."

Dr Ami Sabharwal

VUMC in Amsterdam

Training

It's been a very steep learning curve for all of us

Training was extensive and demanding. Specialist knowledge is needed to operate the MRIdian, as well as a completely new way of working for everyone involved, including dosimetrists, radiographers, physics and clinicians.

"We found ourselves immersed in the day-to-day aspects of how to treat a patient with radiotherapy – what the physics and dosimetry teams do in the background and how radiographers operate the machine – but on the MR linac this all occurs within minutes rather than days whilst the patient lies in the machine"

Dr Andy Gaya

The MRIdian workflow involves a clinician on site during treatment to oversee the daily adaption. This means that clinicians who specialise in prostate must acquire skills in how to adapt to the anatomy of the upper abdomen – and vice versa. Equally challenging was the requirement to acquire skills in magnetic resonance image interpretation and apply them in the setting of a radiotherapy treatment.

"We were not used to planning on MR – it is not one of our routine diagnostic imaging tests. It was a learning curve to recognise tumours on a different modality. Being able to interpret MRI in all areas is an essential part of the training."

Dr Veni Ezhil

The training for the GenesisCare MRIdian took 16 weekends to complete. Much of that was personal time and it was necessary to be extremely efficient and flexible around training given the time commitments of the clinicians. This intensive and comprehensive training was essential to the success of the MRIdian service. The manufacturer, ViewRay, has a well-structured programme and trainers, but the UK team relied heavily on knowledge-sharing with leading healthcare institutions who were working with MRIdian worldwide.

Training took place on a simulator long before the machine was actually installed. It enabled the team to learn together as they tested their process, designing and refining as they went. The extent of this training gave them confidence to move on to more complex and challenging cases within just a few months of starting the service.

"The advantage of doing this in a short time frame was that we learnt the skills and were then able to implement them, consolidating knowledge. Sometimes it's quite hard to maintain momentum when things take a long time to be introduced."

Dr Nicola Dallas

"Contouring, re-contouring every day, working on areas that aren't your speciality, were all initial challenges but proved to be very doable. You need to go to other centres to build relationships and get a body of knowledge; it would take you a long time to do it by yourself and having experience in conventional SABR doesn't give that to you."

Niall McAndrew

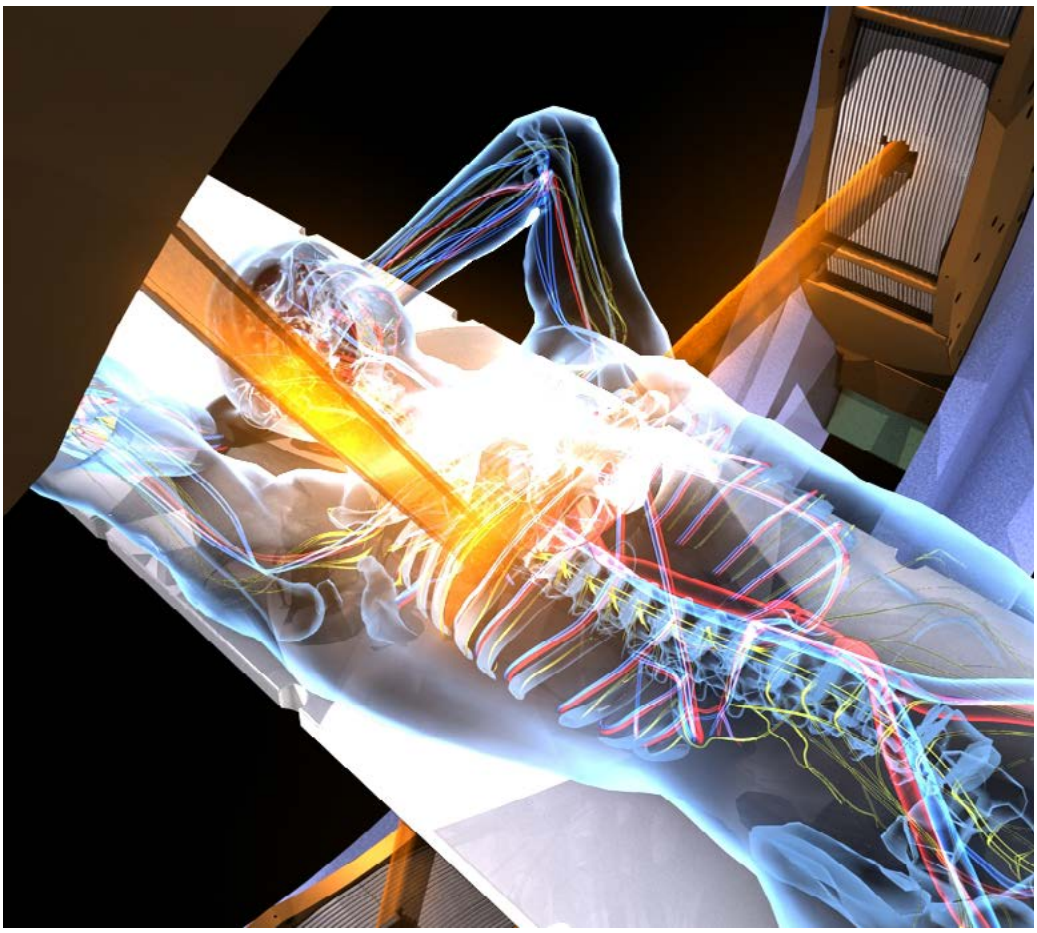


Image: ViewRay

"Dry runs are a key part of training for efficient treatment delivery. Every member of the team needs to be confident in their role and the treatment pathway so that once a patient is on the couch, optimal treatment is delivered safely and efficiently."

Dr Ami Sabharwal

The training programme:

Every member of the team underwent an intensive training programme over a 14-week period prior to the MRIdian going live. It was a disciplined curriculum but there was serious commitment from all involved.

Centres of Excellence

The team undertook these training sessions on site at other MRIdian centres around the world:

- **MR-linac workshop** and working clinically at the Henry Ford Hospital, Detroit
- **Site visits and education** at Heidelberg University Hospital, Miami Cancer Institute, Siteman Cancer Centre, Carbone Cancer Center, University of Wisconsin, VUMC, Amsterdam and Acibadem, Istanbul
- **Doctor credentialing** at VUMC, Amsterdam and Acibadem, Istanbul

ViewRay training

Dedicated training sessions were provided by the MRIdian manufacturer, ViewRay, covering:

- **Applications**
- **Webinar training**
- **Physics**
- **Treatment planning**
- **Treatment delivery**
- **MRI guidance**
- **Prostate planning at VUMC, Amsterdam**

In addition the team undertook **training exercises** supervised by the ViewRay Clinical Applications Team and attended the annual **Users' Meeting.**

Interactive Workshop

These experts generously provided **MRI guidance** workshops:

Dr Frank Lagerwaard – Radiation Oncologist, VUMC, Amsterdam

Dr Mike Bassetti – Radiation Oncologist, Carbone Cancer Center, University of Wisconsin

In addition, the team underwent:

- **MRI safety** training
- **Team-building** sessions and profiling to understand how different personalities would perform in a clinical environment

At the same time comprehensive planning and treatment competency frameworks have now been developed for future dosimetrists and radiographers.

GenesisCare is installing more MR linacs. Subsequent teams will benefit from this knowledge base that is internally embedded.

Credentialing new oncologists

Our clinical strategy now is to train those oncologists who want to offer MRI-guided radiotherapy so that more patients from across the UK can access this incredible innovation. All trained oncologists will be able to undertake planning on the MRIdian and oversee the delivery of the treatment remotely, collaborating with the MRIdian team on site.

Our **credentialing programme** is adapted from our training programme and is delivered by clinicians in their NHS capacity. It includes:

Commitment of a full-day programme on site at GenesisCare in Oxford, incorporating:

Theory

- Understanding how the MRIdian works and the evidence base for 5 fraction prostate, lung and pancreas radiotherapy
- An explanation of the pathway documentation required
- The importance of capturing Patient-Reported Outcomes

Practical

- Introduction to MiM treatment planning system
- Scored planning sessions
- Watch live treatment delivery with plan adaption

Governance

- First three referrals with an allocated MRIdian Consultant to be contoured with the MRIdian team
- Three subsequent prostate, lung or pancreatic referrals will be peer reviewed by the MRIdian team
- Written confirmation of MRIdian credentialing completion provided and reviewed annually as part of practising privileges review process
- 10% of total MRIdian plans are peer reviewed retrospectively by the MRIdian team

"The credentialing is crucial. GenesisCare's approach has never been about exclusivity for doctors, we want to make this available to as many clinicians and therefore patients as possible. But we have to do it in a way that is sensible with a quality assurance approach. We feel we've done things properly so far and we want to keep it that way."

Dr Philip Camilleri

Designing a fully adaptive workflow

It's a completely different way of working

The introduction of MRIdian required a radical change in the radiotherapy workflow. The daily adaptation of treatment is implemented in real time, using a core team of clinicians, radiographers, physics and dosimetrists.

"On a conventional linac, a dosimetrist can spend hours on a complex plan, working in a quiet room, tweaking until they have an optimised plan. With MRIdian you're doing that while the patient is on the bed waiting. It means you have to design an end-to-end process that is quick, robust and high-quality."

Adam Nash

In a standard radiotherapy workflow, a patient will receive a planning CT one to two weeks before the start of treatment. During this time, several steps are carried out by a team of clinicians, radiographers, physics and dosimetrists to produce a treatment plan ready for the patient's first fraction. These steps include contouring the treatment target and organs at risk (OARs), optimising the machine parameters to deliver the prescribed dose to the target while sparing critical structures. These are followed by reviewing the dose distribution, checking the planning process to make sure no errors have occurred and performing an independent dose calculation.

On the MRIdian, as part of the on-table adaptive workflow, the time taken for this process must be reduced safely from days to minutes. In order to achieve this, close inter-disciplinary working between the team is required. They need to undertake a number of complex tasks during each adaptive treatment, increasing the time for each fraction to around one hour.

Setting up a consultant-led MRIdian rota

At its core, the service relies on a MRIdian-trained oncologist to oversee each online adaptive treatment in person to recontour the target where necessary and approve any adaptations to the plan. Although patient assessment and the original treatment plan is the responsibility of the referring clinician, these day-to-day adaptations will often fall to a doctor with a different specialty, depending on who is on the rota.

"I have to focus just as hard on contouring a prostate as my fellow uro-oncologists have to focus on contouring a pancreas. The way we managed that at the beginning was to have plenty of doctors on set"

Dr James Good

"Putting together a MRIdian rota with eight independent consultants from different NHS hospitals, who all have different opinions, priorities and circumstances, is in itself rather challenging. The fact that we've then increased the volumes as quickly as we have is great – because it just means more patients getting access to this treatment."

Paul Gearing

"Every patient is very different because there is a lot of treatment adaption. Compared to traditional radiotherapy, it's a lot more involved and we're working very closely as a team. Communication between the group is important, making decisions quickly while the patient is on the bed, as traditionally you wouldn't have that urgent rush to do that."

Dr Ben George

The rota is designed so that clinicians overlapped and daily contour adaptation could be monitored and assessed by another oncologist.

This approach allowed us to put the MRIdian to its best possible use as early as possible. Ultimately, more patients have benefited as a result.

Our processes were written and iterated with centres of excellence around the world based on their experience. Each step was tested, evaluated with the UK team and revised until we were certain that it was robust. It was the extent of this groundwork that has enabled us to confidently treat some of the most complicated cases in radiotherapy after just a few months.

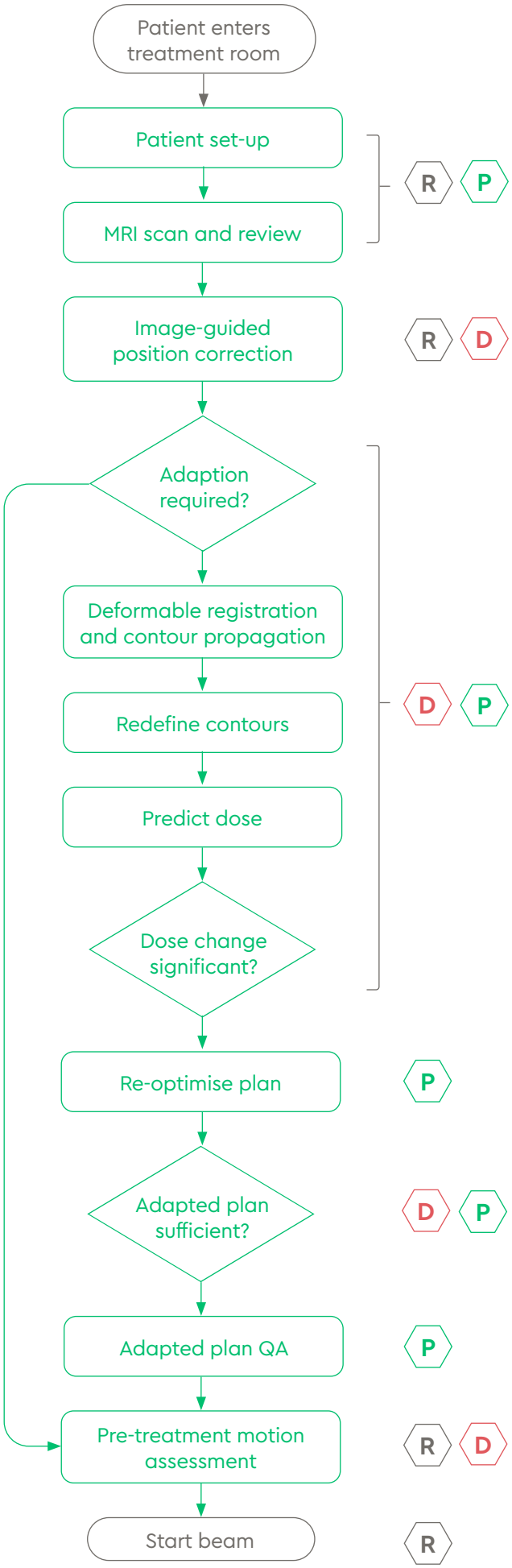
"We took a lot of learnings from VUMC in Amsterdam as well as from the US. We had a lot of input so we could replicate what they did. Then when we started, we were able to gain confidence quickly and begin to develop and find our own way"

Dr Carla Perna

Fig 2: MRIdian workflow diagram
An on-table adaptive workflow based on the ViewRay MRIdian linac with indication of team responsibilities for each step.

KEY

R – Radiographer
P – Physicist or dosimetrists
D – Doctor



"We've been able to treat prostate patients in 40 minutes. We expected it to take 1.5 hours but after six to eight weeks we were able to just go very smoothly through the process. It was due to the preparation and good team-working."

Dr Carla Perna

Reference: Online adaptive radiotherapy using the MR linac. Ben George

Establishing treatment protocols

"We have brought international best practice to bear on what we do and we select cases where the evidence already exists"

Dr James Good

Treatment protocols

Our strategy for the introduction of MRI-guided radiotherapy is to align with international best practice based on evidence-based protocols. We worked closely with other MRIdian centres to ensure that our protocols met internationally agreed standards for safety across each tumour group. There is an increasing international evidence base for MR linac and in particular the MRIdian system. The following is a list of our current protocols which are available for review:

Lung cancers

- We consider SABR treatment on the MR linac for primary lung cancer with curative or palliative intent, to avoid the need for chemotherapy or surgery

Pancreatic and liver cancers

- We use MR-guided SABR for inoperable tumours in the pancreas and as an entirely non-invasive ablative option for primary and secondary liver tumours

Prostate cancer

- We continue to offer radical prostate radiotherapy with 20–37# as per GenesisCare protocol when clinicians decide this is safe to do so
- Patient should be considered for 5# prostate radiotherapy on the MR linac
- We consider SABR for oligometastatic disease to delay hormonal or chemotherapy treatments

Renal cancers

- We would consider MRI-guided SABR for patients with non-metastatic renal carcinoma, for lesions up to 10cm in diameter. We particularly would consider this for patients who are unsuitable for surgical intervention or as an alternative to percutaneous ablation

Further reading and pivotal studies that have informed our protocols is available in our publication, Innovations in MRI-guided Radiotherapy. May 2020.

Patient selection

"It is very important to give the best option to your patients, be honest and open-minded"

Dr Prantik Das

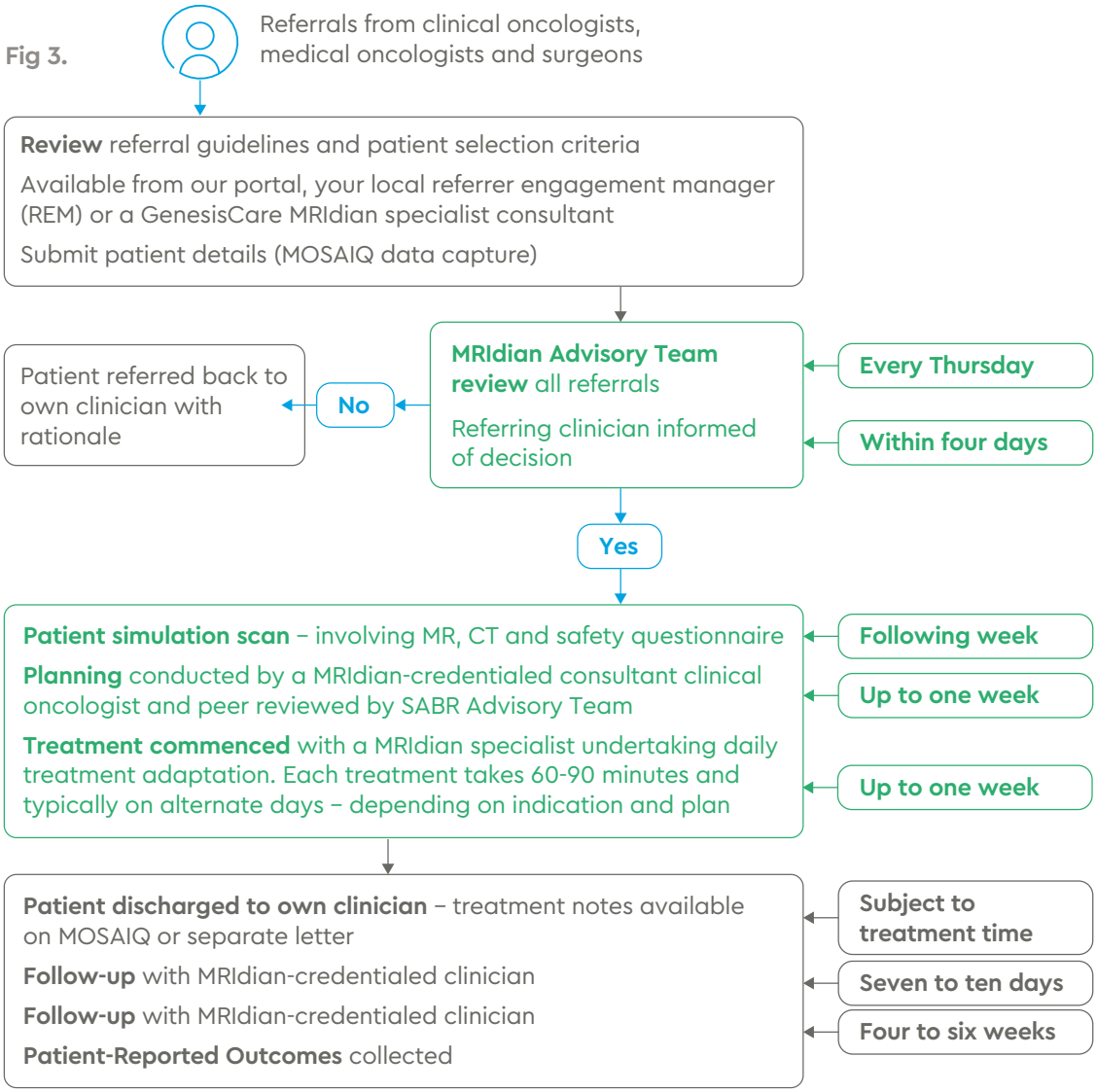
At GenesisCare MRIdian is integrated into the SABR service and is recognised as a tool, not an end in itself. This important distinction guides referrals and ensures that suitable patients receive the treatment that will deliver the best possible outcome.

Potential patients are discussed at our SABR Advisory Group meetings and reviewed based on available evidence. Although the cohort of patients is proving to be fairly wide for MRIdian, for some their needs are better met with a different treatment.

Our SABR Advisory Group meets twice weekly to review patients and is conscious of the need to maintain an efficient service where decisions can be made quickly. Once approved, a patient can normally expect to start their treatment process within a week of their planning appointment.

Our MRIdian referral guidelines and patient selection criteria are regularly reviewed and are available on request.

Fig 3.



The construction and engineering challenge

Preparing for the UK's first MRIdian

Construction started in June 2019, when the foundations were laid, and the facility was complete and ready to accept delivery of the MRIdian in October. The first patient was treated 80 days later. Although this wasn't our goal, this was the fastest installation of any MRIdian globally.

"Good space needs to be considered for not only the equipment but the clinical requirements for day-to-day use"

Steve Bounds, Head of Engineering

GenesisCare is the UK's leading independent provider of radiotherapy, with wide experience of installing linear acclerators. However, the MRIdian presented different challenges. Firstly, the bunker needs to contain not only a linear accelerator but also an MRI cage. Modular bunkers can be built off site and then disassembled and erected faster than a conventional bunker, but can be costly. Based on our experience, we will plan future installations around a conventional bunker due to the specific requirements of an MR linac.

Secondly, there is a lot of accompanying equipment. The delivery for the equipment was around 105 crates. The GenesisCare centre in Oxford is relatively accessible, but the team are already planning how they will deliver this immense volume of equipment for the next installation at Cromwell Hospital in Central London.

The tightly run project benefited from a close and effective relationship with ViewRay. They are a highly specialist supplier with expert project management and were able to meet the timelines for installation, with no compromise on quality.

Oxford is the first of a planned programme of MR linacs across the GenesisCare network and has presented important learnings, such as the construction design and clinical layout of the treatment room. Future bunkers will also be based on a conventional build – rather than a modular bunker – so that they can be tailored to the unique dimensions of the MR linac.

An engineering challenge

At GenesisCare our policy is to self-maintain our equipment as much as possible. This is important so that we can work around our patients and limit the amount of disruption to treatments. The MR linac represents a completely new technology and a new challenge for our engineers. ViewRay engineers are currently supporting engineers to become fully up to speed and confident to maintain the MRIdian without back-up.

"It generally takes around a year and a half to train an engineer for a conventional linac, but this is slightly more complicated with the MRI."

Steve Bounds

"ViewRay are really good to work with. Their project team on the ground went the extra mile"

Niall McAndrew

So far, the technical problems have been limited. In fact, due to the high number of patient referrals, the biggest challenge for our engineers is getting access to the machine between treatments to consolidate their knowledge with a ViewRay engineer.

Section two: Experience so far – 50 patients in 5 months

Section two: Experience so far – 50 patients in 5 months

The report

50 patients in 5 months

By the end of May 2020 we had treated our first 50 patients on the MRIdian.

Treatments started just with prostate in order to ensure the team worked safely during the learning curve. Relatively quickly, the team was confident to move to cancers of the abdomen, pancreas, other sites of metastatic disease, including lung and, most recently, renal cancers.

"MR linac is at the cutting edge of what is currently possible in radiotherapy technology. The type of patients we treat using this modality include many that could not otherwise be safely treated to a similar dose on other platforms"

Dr Andy Gaya

Although the plan was to start treating these more complex cases at a later date, after just a few months it was clear that the process was robust enough to safely start these patients. For many of them, the treatment options were very limited and our patients have travelled from as far afield as Aberdeen.

It is also the case that the COVID-19 pandemic situation drove enquiries from patients and clinicians seeking hypofractionated treatment alternatives to enable patients to be treated quickly with reduced exposure to the unnecessary risk of a clinical environment.

Fig 4. The first 50 patients

Tumour	Stage	No
Prostate	T2	19
	T3	7
Pancreas		8
Liver		2
Other abdominal		6
Pelvis		4
Lung		1
Other		3
TOTAL		50

"I've selected my patients where I've known over time that their condition could not be treated successfully on a conventional linac. For example, SABR for the first time on a central lung is a big issue, SABR for a second time on a previously irradiated field is a challenge."

Dr Veni Ezhil

Cases are selected where the evidence already exists to show the benefits of treatment on the MRIdian. Even so, our clinicians have been surprised at how flexible the MRIdian has proved to be in treating even the most challenging tumours. This includes three individual sites in the liver to be treated at the same time and the first central lung using SABR to treat a previously irradiated field. They have also treated a prostate in a patient with ulcerative colitis, which would never have been possible on a conventional linear accelerator due to toxicity.

A selection of our most interesting case studies are detailed here. GenesisCare is collecting outcome data for all of these patients and looks forward to publishing these in the coming months and years.

"It has opened up a new world of possibility when it comes to using SABR to help patients. I'd hoped that it would but it's very gratifying that it's actually turned out to be the case – and for it to be actually better than I had anticipated."

Dr James Good

"A year ago I would not have recommended any sort of radiation treatment for my patient's recurrence. Now I have treated him. With an extremely positive outcome for the patient"

Dr Carla Perna

"For clinicians to introduce such a complex service, outside of the safety net of the NHS, took a lot of trust in their colleagues. When I first started, I was cautious and slightly anxious, but as time has gone on, I feel more and more confident and I can see that the service is really working, and we're treating more and more patients."

Dr Prantik Das

MRI-guided ultra hypofractionated radiotherapy to the prostate – 9 months later

Dr Philip Camilleri

Case presentation

The patient, a 77-year-old male with prostate cancer, presented with a PSA level 6.8, stage T2cN0M0 with a Gleason score 3+4 = 7 (grade group 2). This gentleman was the first UK patient of GenesisCare to receive treatment on the MRIdian.

Challenges of presentation and choice of treatment

The patient was diagnosed in June 2019 with a multi-parametric MRI scan followed by transrectal ultrasound-guided biopsies. At the time it was felt that stereotactic ablative radiotherapy (SABR) would be an appropriate treatment. His treating uro-oncologist, Dr Philip Camilleri, was one of a group of consultants at GenesisCare undergoing training on MRI-guided SABR radiotherapy in preparation for the installation of the UK's first MRIdian in October. This involved a close working relationship with VU University Medical Center (VUMC) in Amsterdam who already had two identical machines.

It was agreed that the patient would travel to Amsterdam as a guest of GenesisCare for treatment led by the team at VUMC.

MRIdian treatment

He was prescribed 36.25 Gy in five fractions. The treatment was undertaken in September 2019 and completed over alternate days with each session taking approximately 45 minutes to one hour to complete.

At each session, the target was recontoured and the daily plan adapted to allow for daily movement and bowel filling. The importance of live MRI-guided treatment was highlighted on day one when treatment had to be discontinued part way through due to excess wind, making it impossible to safely avoid organ at risk (OARs). The additional part treatment was completed on an additional day.

Results and follow-up

The patient experienced some mild side effects within the first four weeks after radiotherapy but no significant radiation-induced side effects have been recorded.

No patient-reported outcome measures (PROMs) data are recorded for this patient as it preceded the set-up of the UK service in Oxford.

In October, four weeks after treatment, the patient's PSA level had reduced to 4.6. At the end of January, the PSA was 2.3 and in the first week of July 2020 his PSA level was 1.3.

The patient is currently in remission.

Discussion

This was the first UK patient to undertake this ultra hypofractionated treatment. Although he had to travel to Amsterdam, his treatment was completed in five sessions and he found it much easier to complete than expected, with limited toxicities leaving him feeling much better overall. Nine months after treatment, his PSA level continues to reduce as a positive sign of treatment efficacy.

The benefit of MRI-guided radiotherapy to treat prostate cancer in a patient with rheumatoid arthritis on methotrexate

Dr Ami Sabharwal

Case presentation

A 62-year-old male was diagnosed with localised, high risk prostate cancer in November 2019. The patient presented with a PSA level 8.87, stage T3aN0M0 with a Gleason score 3+4 = 7 (grade group 2). The gentleman had a long history of rheumatoid arthritis (RA), which was successfully treated with weekly methotrexate, alleviating all his RA symptoms.

An active semi-retired farmer, he was otherwise healthy and still assisting in farming activities including harvesting hay and felling trees for logs.

Challenges of presentation and choice of treatment

Treatment options were complicated by the fact that the patient had RA, which was being treated with methotrexate. Methotrexate is a radiosensitiser, increasing the toxic effects of radiotherapy.[1] It was therefore discontinued four weeks prior to radiotherapy, for the duration of treatment and for four weeks following radiotherapy. There was concern that the patient's RA would flare up over the three-month period he would need to be off treatment for conventional radiotherapy, equivalent to one month prior, one month during and one month post radiotherapy.

The patient was anxious that he would be unable to continue his farming activities during radiotherapy due to both the side effects of treatment and the potential worsening of his RA symptoms. This would obviously limit his physical activity.

A decision was made to treat on the MRIdian MR linac to deliver stereotactic ablative radiotherapy (SABR) to the prostate in five treatments (over 10 days), rather than the conventional 20 treatments, to minimise time off methotrexate and possibly avoid a flare-up of his RA. With this approach the total time off methotrexate would be maximally 10 weeks, versus a minimum of 12 weeks with conventional radiotherapy treatment.

MRIdian treatment

SABR treatment on the MRIdian was prescribed at 36.25 Gy in five fractions. The aim of treatment was curative.

At each session, daily adaptation was performed to account for changes in the position of the prostate and for variable bladder and bowel filling. Figure 5 and figure 6 illustrate the typical differences seen between the original planning MRIdian scan and that seen on the day of treatment due to day-to-day organ movement. Figure 7 and figure 8 illustrate how these movements were accommodated with the on-table plan adaptation.

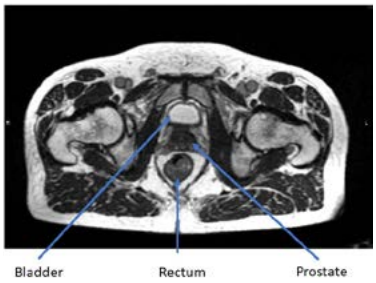


Fig 5

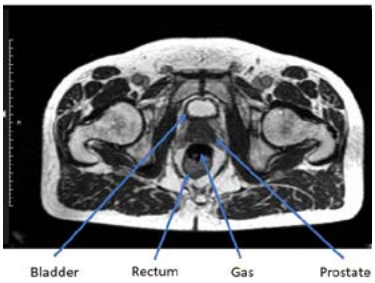


Fig 6

Fig 5: Original planning MRIdian scan

Fig 6: MRIdian scan at fraction 3, prostate position changed due to larger rectal diameter secondary to gas and smaller bladder

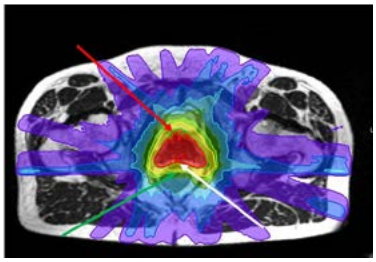


Fig 7

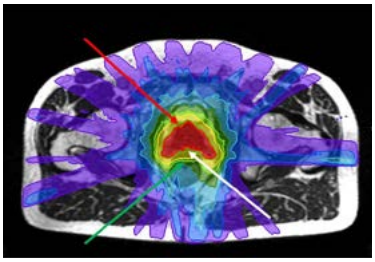


Fig 8

Fig 7: Prostate SABR delivery plan. Prostate volume covered by 95% isodose (green line, red arrow). Tight conformality at rectal/prostate boundary (white arrow), and rapid drop off of high dose (50% isodose, green line, green arrow) to optimise dose delivery to the prostate and limit dose to the rectum, reducing the risk of toxicity

Fig 8: Fraction 3, adapted plan, optimised for anatomy of the day. Prostate volume covered by 95% isodose (green line, red arrow). Tight conformality at rectal/prostate boundary (white arrow), and rapid drop off of high dose (50% isodose, green line, green arrow) to optimise dose delivery to the prostate and limit dose to the rectum, reducing the risk of toxicity

Each treatment including set-up and plan adaptation took 45 to 60 minutes during which time the patient was on the bed. As the patient was local to the treatment centre in Oxford he was easily able to attend the sessions and treatment was completed within two weeks.

Results and follow-up

The patient found the treatment process easier than expected; in fact, he commented that he was unsure if treatment had been delivered as he didn't see or feel anything and experienced no significant bladder or bowel toxicities. Patient-reported outcome measures (PROMs) data collected showed no change with respect to bladder and bowel function between the start and end of radiotherapy. At the end of treatment, there was some improvement in tiredness and low mood reported.

At four weeks post-treatment toxicity check the patient reported urinary frequency (grade 1), but no other bladder or bowel symptoms. At the six-week post-radiotherapy follow-up, his PSA score was 0.09.

There was no deterioration of musculoskeletal function and no flare-up of the patient's RA symptoms.

Discussion

Delivering hypofractionated radiotherapy with the MRIdian reduced the length of treatment by two weeks which meant lesser disruption of methotrexate treatment for rheumatoid arthritis (RA). The patient was surprised at how well he tolerated treatment, allowing him to continue his normal farming activities even during and immediately following treatment without a flare-up of RA symptoms.

Prostate cancer treatment with MRIdian

A meta-analysis of stereotactic ablative radiotherapy (SABR) treatment in prostate cancer by Jackson et al in 2019, including 6116 patients, with a median follow-up of 39 months, demonstrated equivalent biochemical relapse-free survival, with conventional treatment.[2]

A phase 3 randomised control trial, HYPO-RT-PC, Windmark et al 2019, including 1200 patients, randomised to hypofractionated radiotherapy (42.7 Gy in seven fractions) versus conventional treatment (78 Gy in 39 fractions), demonstrated equivalent failure-free survival in both groups (84% in both groups, HR 1.002), with a median follow-up of five years.[3]

Prostate SABR on the MRIdian is associated with low levels of acute and medium term toxicity.

Low toxicity has been reported at one year following SABR on the MRIdian. In 101 patients, no severe (≥grade 3) toxicity was reported. No patients reported any limitation due to urinary symptoms; 97.8% of patients reported no limitation due to bowel symptoms.[4]

References:

1. Spittle, MF. Methotrexate and Radiation. Int J Radiat Oncol Biol Phys 1978 Jan-Feb;4(1–2):103–7.

2. Jackson, W., Silva, J., Hartman, E., Dess, R., Kishan, A., Beeler, W., Stereotactic Body Radiation Therapy for Localized Prostate Cancer: A Systematic Review and Meta-Analysis of Over 6,000 Patients Treated On Prospective Studies. Int J Radiat Oncol Biol Phys. 2019;104(4):778-789.

3. Windmark, A., Gunnlaugsson, A., Beckman, L., Thellenberg-Karlsson, C., Hoyer, M., Lagerlund, M., Ultra-hypofractionated Versus Conventionally Fractionated Radiotherapy for Prostate Cancer: 5-year Outcomes of the HYPO-RT-PC Randomised, Non-Inferiority, Phase 3 Trial. Lancet. 2019;394(10196):385–395.

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A case study of MRI-guided radiotherapy to treat a metastatic prostate cancer recurrence

Dr Carla Perna

Case presentation

A 58-year-old male with metastatic prostate cancer with recurrence in the left obturator nodes previously treated with external beam radiotherapy (EBRT). Due to the complexity of treatment, the patient underwent stereotactic ablative radiotherapy (SABR) using the MRIdian.

At initial diagnosis in 2015, the patient presented with a PSA value of 8, Gleason score 5+5 = 10 (grade group 5), stage T3aN0M0. He underwent radical prostatectomy and lymph node sampling, adjuvant radiotherapy to the prostate bed and androgen suppression.

In September 2017, he had a PSA rise to 0.68 and was found to have recurrent disease in the pelvic side wall, leading to these further lines of treatment and diagnosis over the next three years:

- Docetaxel chemotherapy
- Abiraterone
- A left hemi-pelvic salvage lymphadenectomy – due to recurrent disease with histology – which showed one lymph node with organised calcified fat necrosis and no sign of cancer
- Results of a CT-guided biopsy consistent with metastatic adenocarcinoma with neuroendocrine differentiation. This was then treated with three cycles of Carboplatin and Etoposide chemotherapy
- The patient then received five cycles of Lutetium^{177} PSMA therapy, which was discontinued in January 2020 due to disease progression. A PSMA PET scan completed after cycle five showed that the Lutetium PSMA had reduced the size of the recurrence and he was considered for SABR

The patient was an active gentleman, married with children and working as an engineer.

Challenges of presentation and choice of treatment

The patient had previously been treated with external beam radiotherapy (EBRT) to the prostate bed yet the cancer had recurred in the same area despite several lines of treatment. Although SABR was considered an option, the PSMA PET scan showed that the recurrence was close to organs at risk (OARs), particularly the rectum and the sacral nerve.

MRIdian MRI-guided radiotherapy was therefore chosen due to the complexity of the case and the difficulty of meeting the tolerance constraints of the OARs and of keeping toxicities within the mandatory limits.

MRIdian treatment

Stereotactic ablative radiotherapy (SABR) treatment with the MRIdian was prescribed at 30 Gy in five fractions, to the left obturator nodes. The aim of treatment was to ablate the single recurrence.

The SABR-COMET phase II multicentre trial investigated patients with oligometastatic disease from prostate, breast, lung and colorectum.[1] It did show an increase in survival in patients with between one and five metastases. Median overall survival was 41 months for patients treated with SABR compared to 28 months in the standard treatment arm. Progression-free survival was 12 months in the SABR arm compared to six months in the standard radiotherapy arm.

Treatment took place over a two-week period in March 2020.

At each treatment session, on-table adaptation was performed to optimise the treatment delivery and spare the sacral nerve root. This process from set-up, contouring, plan adaptation and treatment delivery took approximately one hour for each session. The patient was able to travel from his home in Surrey for each appointment in Oxford.

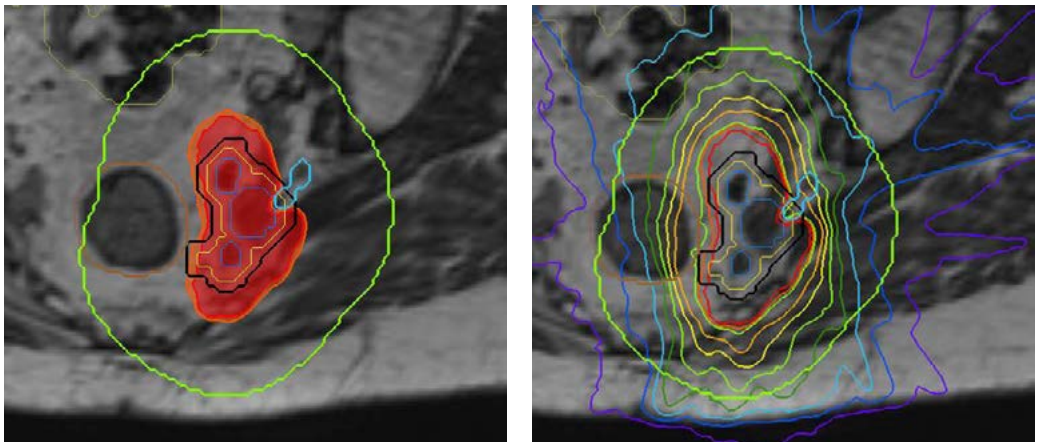

Fig 9 and 10: Planning. 100% isodose in red shaping off sacral nerve root, and orange contour is the rectum remaining tolerance dose of 28.8 Gy. Down to the 50% isodose in green

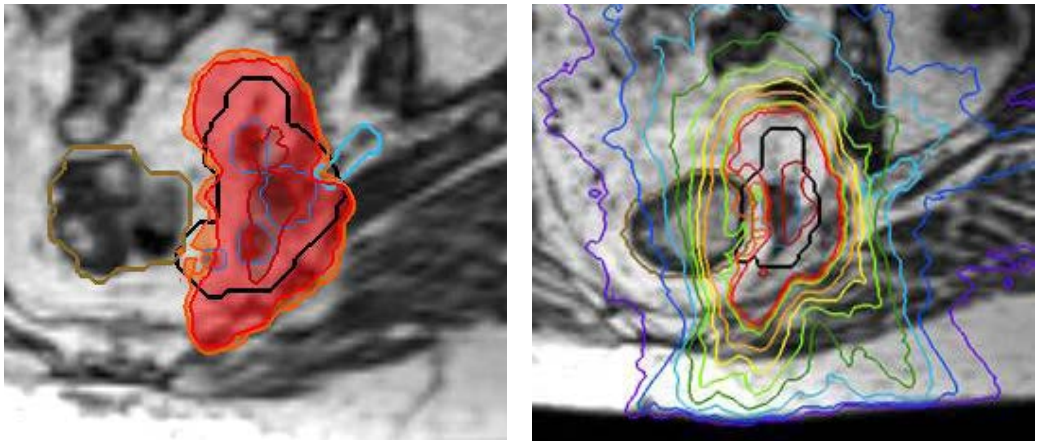

Fig 11 and 12: Fraction 1. Change in rectum position and 120% hotspot over the gross tumour volumes (GTVs)

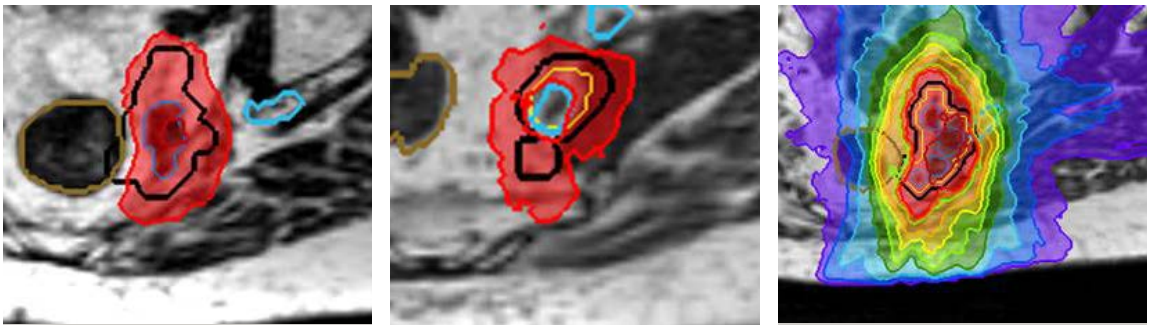

Fig 13: Fraction 3. Hot spot 120% directly in gross tumour volume (GTV)

Fig 14 and 15: Fraction 5. Nerve inside the planning target volume (PTV) being spared the 100% isodose

Results and follow-up

The patient tolerated the treatment well and reported no acute bowel toxicity or other side effects during or post radiotherapy. He was extremely happy with the outcome and also that the treatment has not impacted his quality of life.

At six-week follow-up the PSA value had markedly reduced to 0.11 and 0.3 from the baseline of 0.76 at 3 months follow-up showing a good response to treatment.

Patient-reported outcome measures (PROMs) data continue to be collected for this patient to monitor toxicities.

Discussion

This patient with metastatic disease had undergone most available modalities for prostate cancer and now had limited treatment opportunities for recurrence due to previous radiotherapy, and close proximity of organs of risk (OARs). Using MRIdian MRI-guided radiotherapy it was possible to use better tissue visualisation and live daily, on-table plan adaptation to limit toxicity and treatment aims were achieved with minimal impact to the patient's quality of life.

References

1. Palma, D., Olson, R., Harrow, S., Gaede, S., Louie, A., Haasbeek, C., et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet. 2019;393(10185):2051–2058.

A case study of MRI-guided radiotherapy to treat prostate cancer in a patient who was a main carer of his wife

Dr Prantik Das

Case presentation

An 82-year-old man with intermediate risk localised prostate cancer was unable to undergo conventional radiotherapy due to family circumstances.

He was already under the care of a urologist in his hometown of Derby and diagnosed with stage T2cN0M0, a Gleason score 4+3 = 7 (grade group 3) and PSA value of 18. The patient had been started on bicalutamide but was struggling with the side effects of tiredness and painful enlargement of the breast. He also had a previous history of high cholesterol and was being treated with statins.

External beam radiotherapy (EBRT) was now being considered as a next line of treatment by his urologist.

A retired company owner, the gentleman is now a full-time carer for his wife who suffers from a chronic debilitating health condition.

Challenges of presentation and choice of treatment

Conventional EBRT radiotherapy for this patient would typically involve 20 to 37 fractions over four to seven and half weeks. The patient had decided against this treatment as he felt that travelling to hospital for several weeks would not be possible with no one to care for his wife. Instead, he had opted for long-term oral endocrine treatment, but this was now affecting his quality of life.

Stereotactic ablative radiotherapy (SABR) was then considered as a recommended treatment for low and intermediate risk prostate cancer. Treatment can be completed in five fractions which would allow the patient to care for his wife.

The option to deliver this SABR on the MRIdian offered additional benefits. The daily adaption can allow for intra and inter fractional movement of the prostate and organs at risk (OARs), improving treatment accuracy and therefore reducing toxicity to healthy tissue. This could help to achieve a better quality of life (QoL) for this patient. It would also allow him to stop long-term endocrine treatment which was also adversely affecting his QoL.

MRIdian treatment

The patient was treated with five fractions of SABR using the MRIdian for MRI-guided treatment delivery, with the aim to achieve maximum disease control or be curative. Treatment commenced in December 2019 and was given on alternate days to meet the patient's requested pre-Christmas completion date.

SABR treatment on the MRIdian was prescribed at 36.25 Gy in five fractions. During each treatment session, daily adaptation was performed to account for changes in the position of the prostate due to variable bladder and bowel filling. It has been well recognised that the prostate moves during the course of radiotherapy.

Figure 16 and figure 17 illustrate the typical interfraction movement as seen on the MRI scan. Figure 18 and figure 19 demonstrate the daily changes of the patient's internal anatomy whilst figure 20 and figure 21 show the adaptive radiotherapy plan.

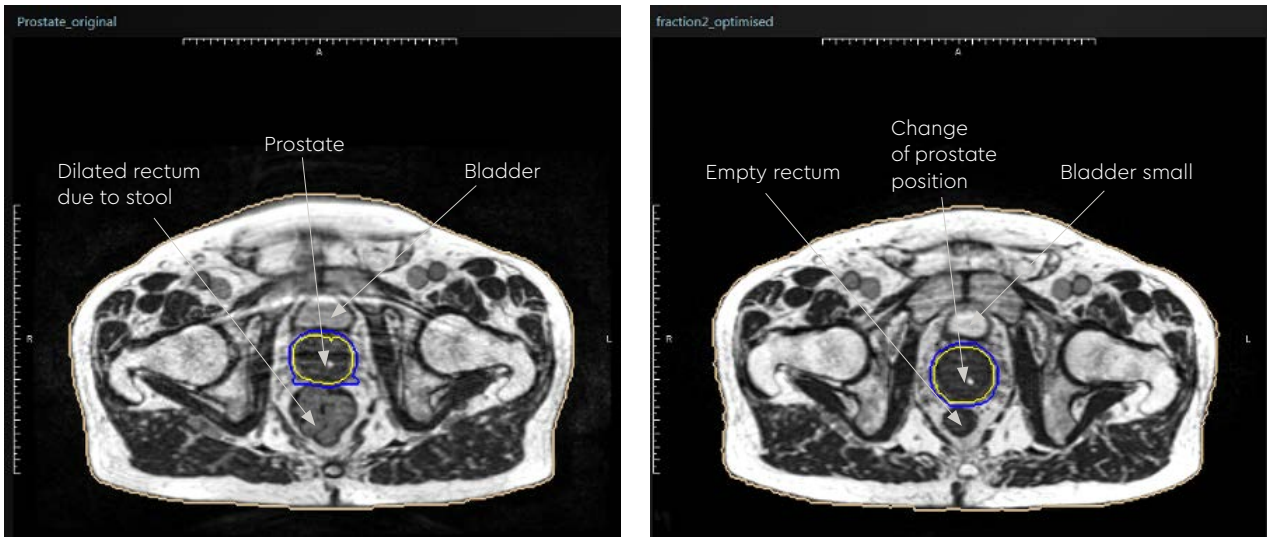

Fig 16: Internal anatomy during the planning MRI

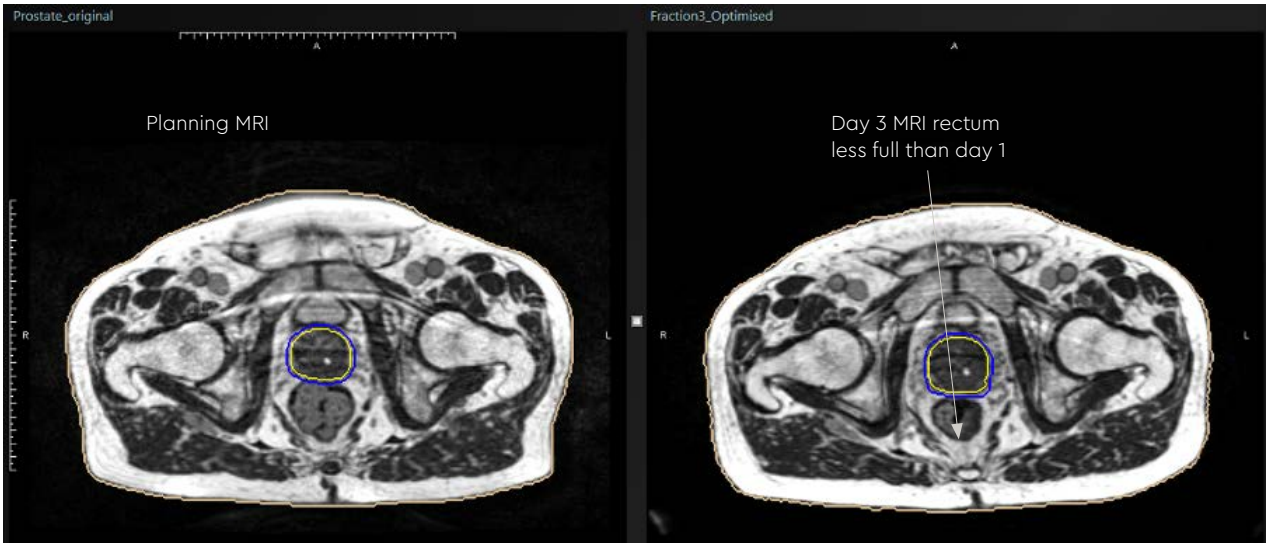

Fig 17: Internal anatomy during first fraction of treatment

Fig 18: Changes in internal anatomy demonstrated by a smaller rectum on day 3 compared to the planning scan

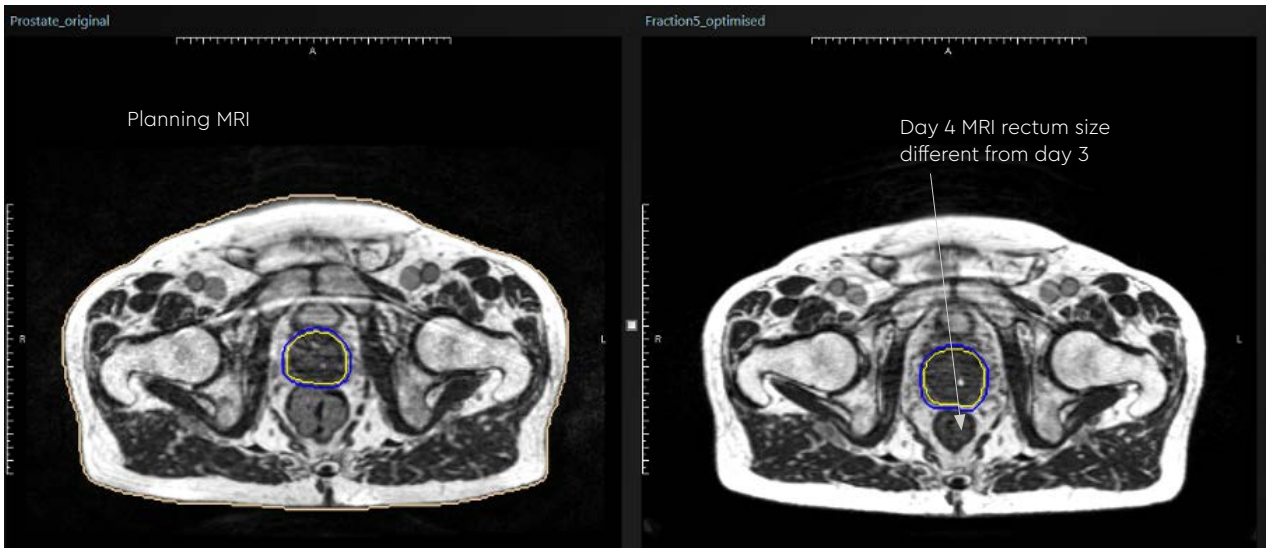

Fig 19: Changes in internal anatomy demonstrated by a different rectum size on day 4

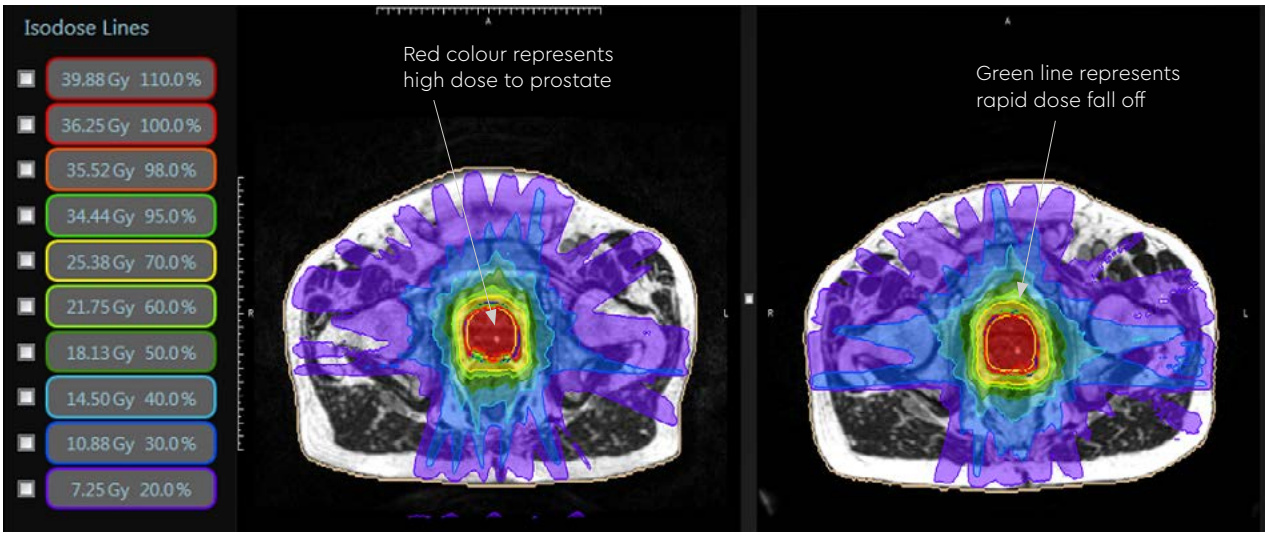

Fig 20: Radiotherapy plan

Fig 21: Plan adaptation. Tight conformality at rectal and prostate boundary is demonstrated by the arrow. Rapid reduction of high dose optimises dose delivery to the prostate and limit dose to the rectum, reducing the risk of long term toxicity

Each treatment session, including set-up and plan adaptation, took 45 to 60 minutes during which time the patient was on the bed.

Although the patient lived in Derby, he was able to travel to the GenesisCare centre in Oxford each day for treatment and private transport was provided as part of his care.

At each session, the target was recontoured by the treating clinical oncologist and the plan adapted daily before treatment. This was found to be necessary due to the degree of movement and shifting of the prostate influenced by bowel and bladder filling.

This daily adaptive process took an average of 54 minutes for each of the five SABR treatment sessions.

Results and follow-up

Minimal side effects were recorded, with grade 1 bowel and grade 1 urinary toxicities which settled very quickly after treatment. In fact, these side effects were so minimal that the patient was concerned that treatment might not be effective.

Post-radiotherapy, his endocrine treatment was stopped, the side effects of tiredness had reduced within three weeks and he was feeling significantly better. At five months follow-up, the patient's PSA value had decreased to 1.6 from 18 at the start of radiotherapy treatment.

The patient is continuing to provide patient-reported outcome measures (PROMs) data.

MRI-guided radiotherapy allows technology to be extended for use both in radiotherapy planning and for adaptations during treatment. The advantages of this are numerous – firstly, it can allow greater accuracy in delineating clinical target volumes and organs at risk.[1,2] This in turn could lead to smaller volumes being irradiated which may reduce both acute and long-term radiation toxicity. Furthermore, rather than having a 'snapshot' of the anatomy, as would be provided by traditional IGRT (image-guided radiotherapy) such as a cone beam CT, this allows direct visualisation of the relevant area during the radiotherapy treatment.

The MRIdian MR linac enabled this patient to undergo curative radiotherapy treatment for prostate cancer with minimum impact on his day-to-day responsibilities as a carer for his wife. This was achieved with minimal short-term toxicities and in doing so, it was possible to reduce the side effects of long-term hormone treatments, greatly impacting the patient's quality of life.

This gentleman was the first patient to be treated on the MRIdian at our GenesisCare centre in Oxford and this was also the first ever MRIdian treatment in the UK. We are delighted we could provide a positive outcome for him and his wife.

References:

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A case study of MRI-guided radiotherapy to treat prostate cancer in a gentleman with a left prosthetic hip

Dr Nicola Dallas

Case presentation

A 74-year-old male with intermediate risk prostate cancer. The patient had a PSA value of 9.8 and a multiparametric MRI scan revealed a left peripheral zone tumour at the apex of the prostate along with the known previous left total hip replacement.

The patient was subsequently diagnosed with a prostate adenocarcinoma stage T2bN0M0 with a Gleason score 3+4 = 7 (grade group 2). He was started on bicalutamide hormone treatment. At the time of presentation, he was also taking tamsulosin to reduce his urinary tract symptoms.

Despite the hip replacement this gentleman remained very active – walking and running daily and continuing to work.

Challenges of presentation and choice of treatment

A hip replacement ordinarily produces significant artefact on a planning CT and diagnostic MRI. This presents particular challenges for conventional radiotherapy, making it difficult to visualise and contour the prostate gland for radiotherapy planning. This inability to accurately define the prostate gland in turn increases the potential toxicity to surrounding structures during treatment.

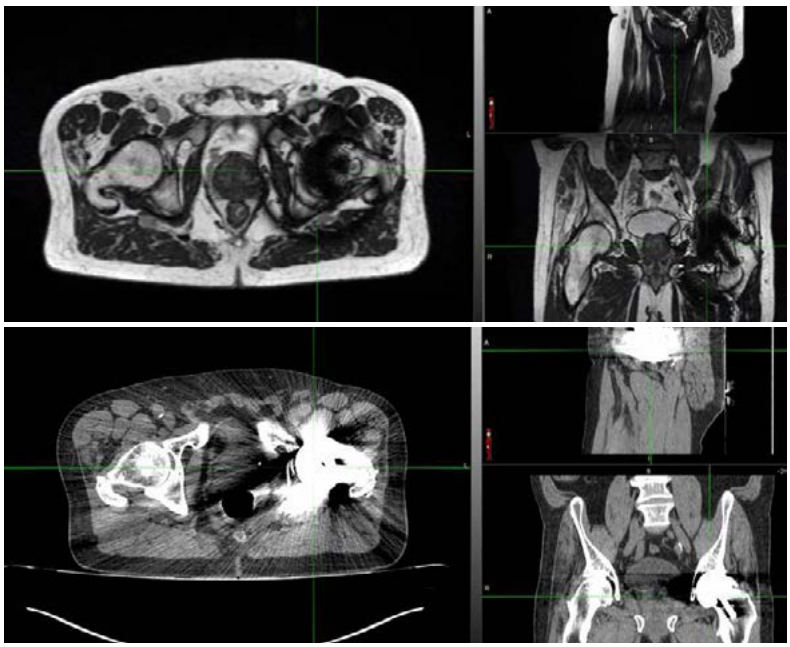


Fig 22: Planning scans of the patient. The top image shows MRI planning images using 0.35 T MRIdian displaying minimal artefact around the left prosthetic hip. The bottom is a CT planning scan of same patient showing significant artefact and obscured prostate views

Prostate brachytherapy was not considered a suitable treatment alternative to external beam radiotherapy here because of this gentleman's significant lower urinary tract symptoms, and consequent use of tamsulosin. Brachytherapy can cause a significant and prolonged flare of genitourinary symptoms, and possible urinary retention, in patients with poor functional parameters pre-treatment.

Experience in other centres, such as the VU University Medical Center (VUMC) in Amsterdam, had already demonstrated that a hip prosthesis produces minimal interference on the imaging function of the MRIdian MR linac, enabling accurate localisation of the prostate gland. The MR linac technique then combines daily adaptation and real-time visualisation to facilitate a significantly reduced treatment margin, thereby minimising rectal dose and associated toxicity.

The patient therefore opted for treatment with ultra hypofractionated radiotherapy on the MR linac, on the basis that with improved localisation of the prostate it could minimise potential toxicity and long-term side effects to his rectum and bladder.

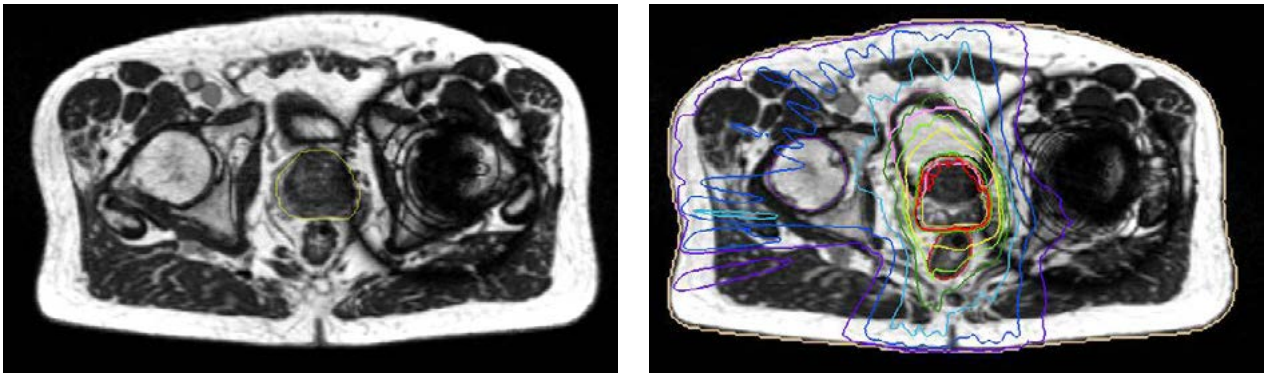


Fig 23: The MRIdian treatment plan with prostate contour on the planning MRI scan shown on the left and the prostate plan achieved on the right

MRIdian treatment

Treatment was prescribed at 36.25 Gy in five fractions on the MRIdian. The aim of treatment was curative.

Treatment commenced within two weeks and was delivered in five fractions over two weeks. During this time, the patient travelled to each fraction from his home in Birmingham. At each session, minimal adjustments were made to the clinical target volume and the organs at risk (OARs) were recontoured for their daily position. Most fractions were completed within a 40-minute timeframe including patient set-up.

In the event, the imaging quality of the MRIdian's in-built MRI function proved to be excellent, facilitating accurate organ visualisation and targeting. The patient, complete with prosthetic hip tolerated treatment on the MR linac, confirming the experience of other centres.

Results and follow-up

At the time of writing this case study, it was too soon to assess side effects and treatment outcome.

The patient will complete patient reported outcome measures (PROMs) questionnaires, but at the time of writing he has tolerated the treatment well and reported no significant impact on lifestyle, other than travelling to and from treatment.

Discussion

Radiotherapy treatment to the prostate gland is possible for patients who have a hip prosthesis using the MRIdian MR linac. This technique provides high quality visualisation of the prostate and is well tolerated. Future data will be reviewed to measure the full benefit of this therapy in reducing toxicities and improving quality of life.

A case study of MRI-guided radiotherapy to a sub-diaphragmatic node in the upper abdomen

Dr Philip Camilleri

Case presentation

A 52-year-old female with metastatic renal carcinoma. At the time of referral for stereotactic ablative radiotherapy (SABR) she had oligoprogressive disease in a single lymph node beneath the right diaphragmatic crus (figure 1).

The patient was initially diagnosed in October 2018 when she also underwent an open right radical nephrectomy confirming the presence of renal clear cell carcinoma with rhabdoid change, stage T3bNxMx. Further investigation revealed the presence of multiple pulmonary metastases and she was commenced on nivolumab and ipilimumab immunotherapy treatment. Her metastatic disease had been completely controlled with no evidence of growth until a routine check CT scan identified an enlarging right upper abdominal node adjacent to the right diaphragmatic crus. At the same time, she developed right upper abdominal pain which was thought to possibly be due to the nodal growth but also possibly due to gallstones which she was also known to have.

She was otherwise enjoying an active lifestyle which had been mostly unchanged by her disease.

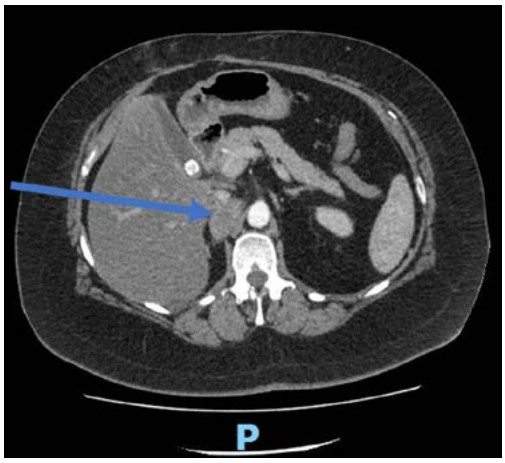


Fig 24: Pre-treatment CT scan showing right upper abdominal node measuring 25mm on 10th January 2020

Challenges of presentation and choice of treatment

Radiotherapy was an option to achieve local disease control. However, this was a complex case due to the close proximity of the liver and small bowel, and the movement of these organs at risk (OARs) with respiration.

The opportunity to treat this patient with SABR using the MRIdian MRI-guided system was reviewed with the SABR Advisory Team at GenesisCare.

With its integral MR scanner and real-time imaging, MRIdian offers the capability of good soft tissue visualisation in the upper abdomen as well as allowing clinicians to account for the location of small bowel and other significant OARs, adapting the radiotherapy plan on a daily basis. This adaptive radiotherapy, together with the breath-hold and automated beam gating function of MRIdian, allows a high dose to be safely delivered to the target.

MRIdian treatment

Stereotactic ablative radiotherapy (SABR) treatment on the MRIdian MR linac was prescribed at 40 Gy in three fractions. Treatment sessions were carried out on alternate days and were completed at the end of February.

The dose prescribed was in line with the UK SABR consortium guidance for stereotactic radiotherapy to involved nodes.

At each session the plan was recontoured and the daily plan was adapted to match the position of the target node as well as the surrounding organs at risk, specifically the small bowel and liver. This was important to ensure the dose to organs at risk (OARs) was kept to an absolute minimum. The patient was also required to use the breath-hold visualisation, to enable the automated beam gating. Each treatment session took approximately 45 minutes, including contouring and plan adjustment.

Results and follow-up

The patient noted very few treatment side effects. She had grade 1 fatigue lasting two weeks and no nausea, vomiting or bowel disturbance.

Patient-reported outcome measures (PROMs) are collected from baseline and show that although she had recorded moderate fatigue prior to her SABR treatment and on the day of her final fraction, four weeks and three months post treatment she recorded no fatigue.

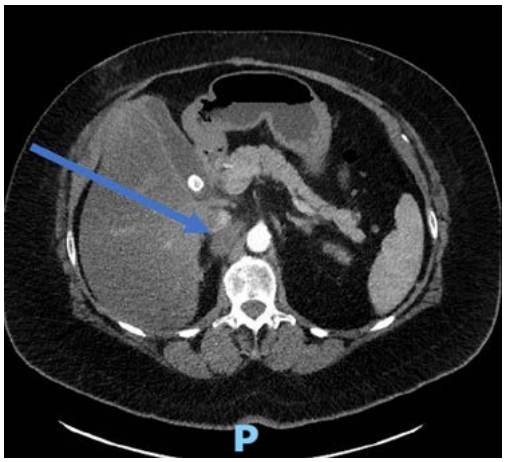


Fig 25: Post-treatment CT scan (19mm) on 12th May 2020 10 weeks after completion of SABR

Other PROMs show no change from baseline in pain, gastric symptoms, intestinal symptoms, sexual functions or emotions.

A follow-up CT scan at 10 weeks after SABR treatment showed a reduction in size of the node.

Discussion

SABR using the MRIdian MR linac allowed safe delivery of a high dose, while limiting toxicity to OARs. In the event, this was found to be a straightforward treatment approach. The patient was delighted to have completed her treatment so quickly and with almost no effects apart from mild fatigue.

A case study of MRI-guided radiotherapy to treat multiple liver metastases

Dr James Good

Case presentation

A 64-year-old lady with a history of HER2 negative ER+ breast cancer. She initially presented with stage pT2N1M0 disease and had previously undergone wide local excision and post-op radiotherapy, chemotherapy and endocrine therapy. She relapsed with three liver metastases on FDG PET and MRI and on the basis of the SABR COMET trial results, and a preference to avoid surgery, was referred for stereotactic ablative radiotherapy (SABR).

Challenges of presentation and choice of treatment

The challenge here was the number of metastases. Two of them were in a position not amenable to percutaneous radiofrequency ablation, and given that breast cancer can recur in other tissues as well as liver, surgery was likely not to be the optimal approach. The lesions were positioned in different segments of the liver, making it challenging to treat with conventional SABR due to the need for an internal target volume (ITV), leading to an increased mean liver radiation dose and therefore potentially reduced dose to the tumours.

MRIdian treatment

The patient accepted treatment on the MR linac despite being apprehensive about the treatment time. The lesions were readily visible on the MRIdian planning scans with IV liver-specific contrast (figure 26). She completed treatment as planned, and we were able to deliver 50 Gy in five fractions to all three lesions. During the adaptive replanning process we could see that the gross tumour volumes (GTVs) were decreasing in size as SABR proceeded. She has also continued with second line endocrine therapy.

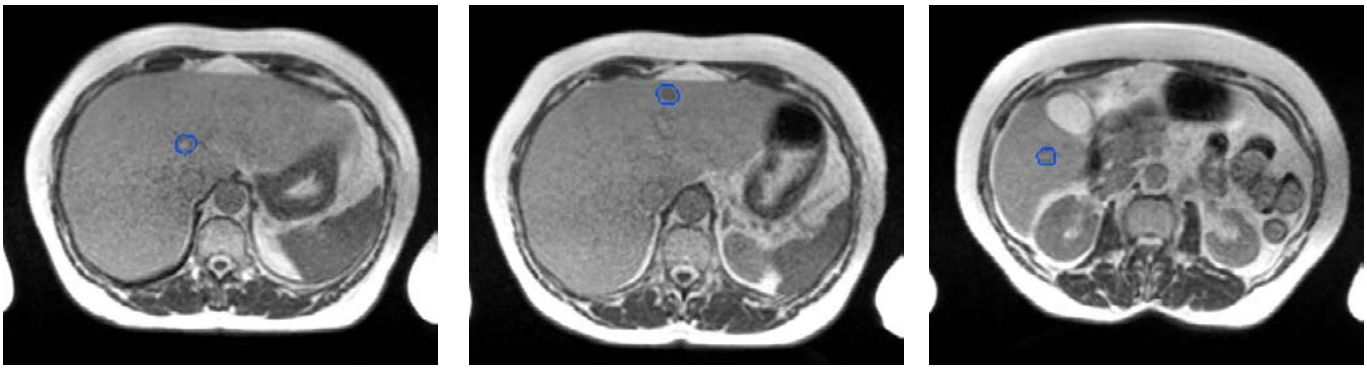


Fig 26: Pre-treatment MRIdian planning scans showing three small, scattered liver metastases

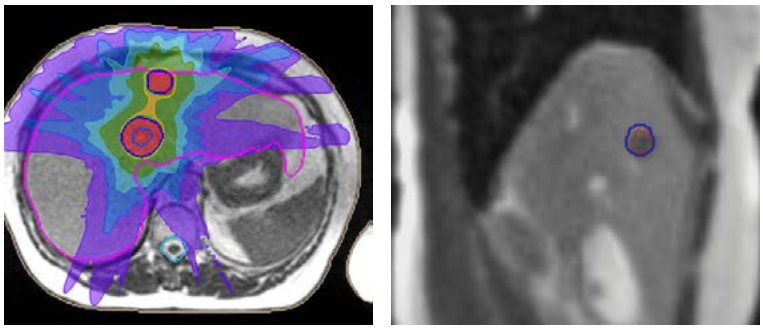


Fig 27: MRIdian SABR plan, showing tight dose distributions across two of the three tumours

Fig 28: Treatment tracking image, which empowered the patient to participate in her own treatment

Results and follow-up

The patient did develop some rib tenderness related to radiation dose to the most peripheral lesion, but this settled with simple analgesia and time. MRI scan at three months showed the tumours were almost completely clear and a further scan at six months showed no active cancer. The patient requires ongoing endocrine therapy to control her disease.

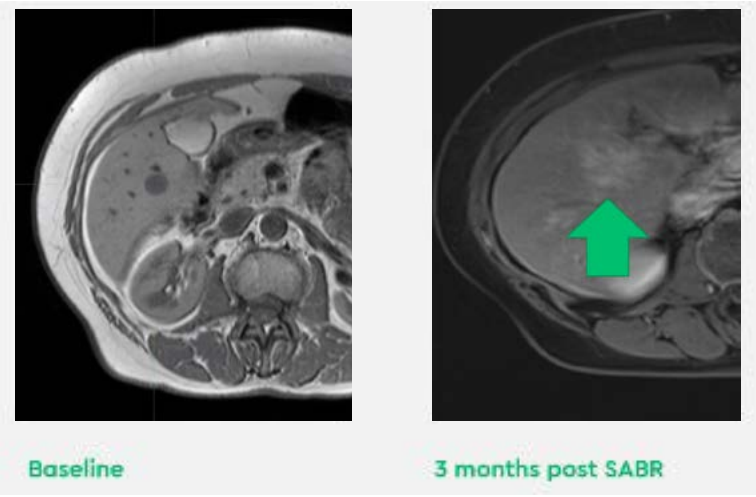


Fig 29: Post-treatment MRI scan, showing a well demarcated ablation zone

Discussion

The improved soft tissue definition, beam gating and adaptive replanning made possible by MRIdian allowed an entirely non-invasive approach to ablating this lady's liver metastases. MRI-guidance added value through greater confidence in delineating and tracking gross tumour volumes smaller treatment margins and maximising the ablative radiation dose.

A case study of MRI-guided radiotherapy to treat a pancreatic tumour

Dr Andy Gaya

Case presentation

A 47-year-old female with oligometastatic disease and a local recurrence of pancreatic ductal adenocarcinoma, adjacent to superior mesenteric vessels.

The patient was originally diagnosed in 2018 with moderately differentiated disease in the uncinate process, which was borderline resectable and in close proximity to the superior mesenteric vein. She presented with obstructive jaundice in late June 2018 and was treated with a metallic stent inserted to the central bile duct. Neoadjuvant Folfirinox chemotherapy commenced in July with stable disease after four cycles. This was followed by chemoradiotherapy to the uncinate process tumour and subsequently a Whipples resection and partial gastrectomy at the end of December that year. This identified poorly differentiated (grade 3) adenocarcinoma, stage T2N1M0 with R1 SMA margin, the positive margin was clipped and adjuvant Folfirinox was commenced from February to May 2019.

In September 2019 there was a local recurrence adjacent to the superior mesenteric vessels and the patient was given gemcitabine and nab-paclitaxel chemotherapy, with a partial response.

The patient was fit and healthy with two small children. A social smoker, she drank alcohol in moderation and had been diabetic since the onset of cancer to her pancreas.

Challenges of presentation and choice of treatment

This was a difficult case of incurable disease in a young woman with a young family. The pancreatic tumour was initially inoperable and then recurred within months of surgery.

The patient had received previous radiotherapy to the pancreas and therefore the surrounding normal tissues were already near tolerance. The only option for retreatment with a meaningful biological effective dose (BED) would be to use the MRIdian, which would accurately account for the varying position of the bowel and duodenum each day. This would be achieved by adapting the treatment plan at each session and using the respiratory beam gating during treatment.

MRIdian treatment

SABR treatment on the MRIdian was prescribed at 40 Gy in five fractions, with the aim of achieving local control. This was completed at the end of January 2020.

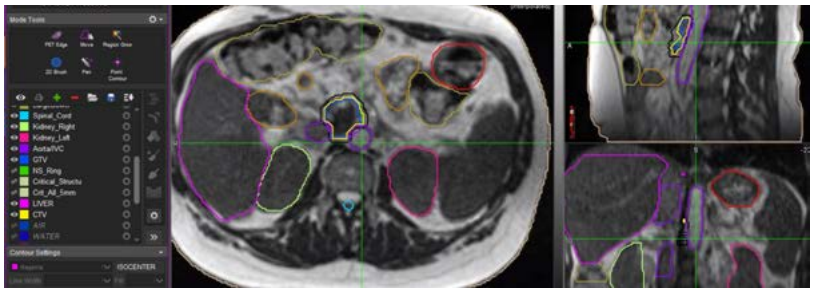


Fig 30: Anatomical location of the recurrent tumour and the critical organs at risk

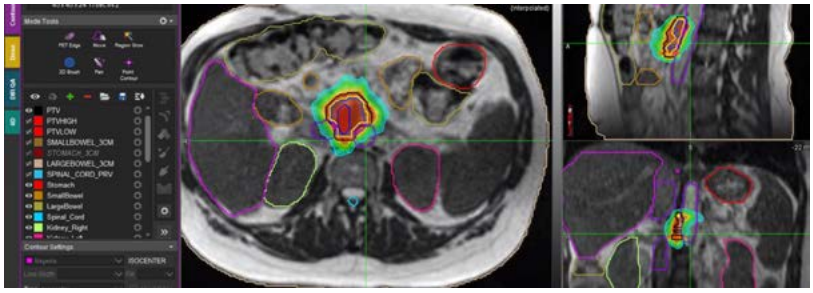


Fig 31: Radiation treatment plan down to 50% isodose

Treatment commenced within two weeks and was delivered over five days over a two-week treatment period. The patient travelled from her home in Hertfordshire for daily treatment. At each session the target and organs at risk (OARs) were recontoured and the plan was optimised to minimise dose to normal tissues. Due to complexity, treatment took 90 – 120 minutes to complete from set-up, plan adaptation and treatment delivery, during which time the patient remained on the bed.

She was also required to participate in the breath-hold function of MRIdian, essential for automatic beam gating to achieve smaller margins.

In March, the patient was re-commenced on chemotherapy with gemcitabine and nab-paclitaxel, which was completed at the end of April.

Results and follow-up

The patient tolerated her treatment well, with only some side effects; fatigue (grade 1), nausea (grade 2) and vomiting (grade 1). Overall she found the treatment had minimal impact on her lifestyle and was very happy with all aspects of her care.

She found the breath-hold visualisation in particular very empowering.

Patient-reported outcome measures (PROMs) data continue to be collected.

In June, coeliac and left supraclavicular (SCF) node biopsies was performed and revealed a new node in the SCF and porta hepatitis, which unfortunately showed distance progression. She is now receiving systemic therapies.

Discussion

Retreatment radiotherapy, to a full dose, even in difficult areas like the pancreas is possible with the MRIdian MR linac. For this patient, there was an opportunity to target local disease control when treatment options are limited, with minimal impact on her lifestyle.

A case study of MRI-guided radiotherapy to treat a central lung tumour

Dr Veni Ezhil

Case presentation

A 72-year-old male with a local recurrence of small cell lung cancer, five years after initial diagnosis. The patient was diagnosed in May 2015 with T3N1M0 limited stage small cell lung cancer and underwent systemic chemotherapy with six cycles of carboplatin and of etoposide with partial response. He was also given radical thoracic radiotherapy, 64 Gy in 32 fractions and prophylactic cranial irradiation, 25 Gy in 10 fractions.

In December 2019, a routine chest CT scan showed an area of relapse in the right upper lobe (RUL). Staging with PET confirmed a 1.8cm area of relapse in the RUL with no mediastinal nodes or metastatic disease. MRI brain screening was negative. A biopsy confirmed small cell lung cancer. He was re-challenged with four cycles of carboplatin and etoposide completed in February 2020. A PET scan showed stable disease and no evidence of new disease elsewhere.

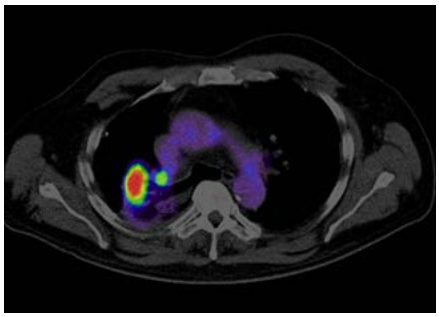


Fig 32: PET/CT image of recurrent tumour in the right lung

The patient, a retired fireman, was otherwise very fit with a regular exercise route and enjoyed long distance motorcycle rides.

Challenges of presentation and choice of treatment

Local relapse of a small cell lung cancer five years after diagnosis, with no metastatic disease. It was especially challenging due to the central location of the tumour and limitations for thoracic reirradiation of an in-field relapse.

Several treatment options were reviewed for this patient. These included:

- Surgery involving a pneumonectomy to ensure a complete resection. The risks of this approach included the potential complications of a major surgical procedure, loss of lung capacity in a fit and active person and the added risk of COVID-19 (at the time of treatment in early 2020)
- Reirradiation on a conventional linac, either as 45 Gy in 15 daily fractions or 45 Gy in 30 twice-daily fractions. Less biological effective dose (BED), compared with SABR. Also involved more clinic visits and risk to the patient during the COVID-19 pandemic

- Stereotactic ablative radiotherapy (SABR) on an MR linac with the aim to deliver a higher BED to maximise local control. The additional features of the MRIdian MR linac would ensure a smaller treatment volume due to gated breath-hold delivery. Daily recontouring would account for changes in position of the target and OARs and plan adaptation would aim for good target coverage, keeping all OARs in tolerance with every fraction. These combined to deliver lower toxicity [1,2]

For these reasons the selected treatment option was SABR on the MRIdian MR linac, with a prescribed dose of 50 Gy in eight fractions. Treatment aims were to maximise local control at the only site of relapse, and reduce the risk of further disease progression.

MRIdian treatment

The patient started treatment in March within two weeks and received eight treatments delivered on alternate days. The patient travelled from Southampton to Oxford for each treatment. At each session, the target and organs at risk (OARs) were recontoured and the plan re-optimised prior to the fraction being delivered.

In the event, the set-up time took approximately seven minutes. The contouring took an average 17 minutes to complete, including the target and OARs and applying the required Boolean operations and rules. It took a further six minutes to check and preview the treatment area.

Treatment delivery itself took around 23 minutes including the gating, when the MRIdian automatically interrupted the beam to avoid OARs or if the target moved out of field. The patient was required to participate with the breath-hold delivery, which he tolerated very well, enabling a shorter time spent on the bed.

Fig 33: Daily re-contouring of a patient with central lung tumour. MRI scans from fraction 1 and fraction 5 show the extent of movement and variation and subsequent re-planning during adaptive treatment

Results and follow-up

The patient tolerated the treatment well with no acute toxicity, aside from grade 1 fatigue. He remained well at the four-week review and reported no toxicity. Patient-reported outcome measures (PROMs) recorded at baseline and at the end of treatment have indicated no side effects and the patient continues to participate in PROMs data collection.

A PET/CT scan in July was delayed as the patient had a fall.

Further follow-up CT scans are scheduled at three-monthly intervals to monitor disease relapse and any evidence of late toxicity.

Discussion

The MRIdian MR linac enabled complex radiotherapy involving a central lung tumour and re-irradiation of a field. Early feedback shows this was achieved with limited toxicity. Local disease control and the effects on disease progression will now be closely monitored to see if the higher biological effective dose (BED) has an effect on outcome.

The patient was able to tolerate the treatment and breath-hold feature particularly well, possibly because he was fit and active.

References:

1. Finazzi, T., Haasbeek, C., Spoelstra, F., Palacios, M., Admiraal, M., Bruynzeel, A., et al. Clinical Outcomes of stereotactic MR Guided adaptive radiation therapy for high-risk lung tumors. Int J Radiat Oncol Biol Phys. 2020;107(2):270 -278.

2. Finazzi, T., Palacios, M., Spoelstra, F., Haasbeek, C., Bruynzeel, A., Slotman, B., et al. Role of On-Table Plan Adaptation in MR Guided Ablative Radiation Therapy for Central Lung Tumors. Int J Radiat Oncol Biol Phys. 2019;104(4):933 -941.

One focus, our patient

Patients are very interested in new technology and how it will benefit them. For example, prostate cancer patients are very positive about the fact that they can have treatment in five visits – instead of 20 – and with reduced toxicity. For others, who perhaps have fewer treatment options available, they can be optimistic about the fact MRIdian is offering them something they wouldn't otherwise have. For other patients there may be fewer treatment options to consider, but they are able to be optimistic about the difference it could make them.

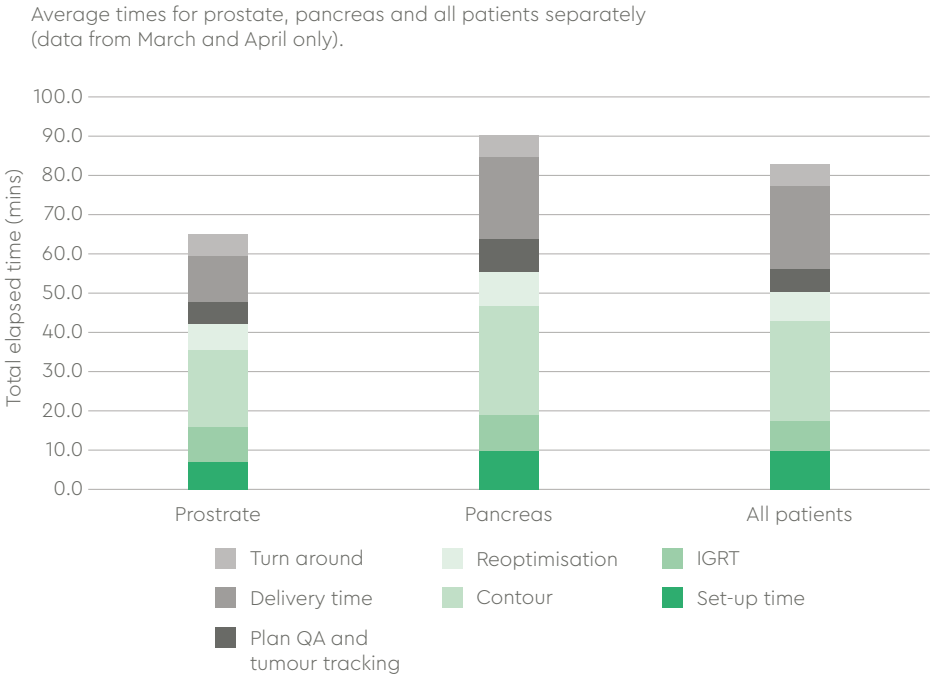
The experience

There are some considerations to the treatment, however, and the MRIdian service has been designed taking account of these so patients have the best possible experience.

Length of treatment

One of the main challenges is the length of each treatment session. In the case of a complex abdominal treatment the patient can be in the MR linac for more than an hour which can understandably be hard for them. It is difficult to reduce this because the treatment is so complicated, however, we have been surprised at how well patients tolerate this.

Fig 34. MRIdian treatment timing data



Some patients participate in breathing control through the use of a monitor in the MR linac room which they view through specially designed glasses. They visualise their tumour and, by controlling their breathing, they can accurately position their tumour within a defined boundary, which activates the beam. Many patients have likened this method of beam-gating to a computer game and they feel in control of their treatment.

Claustrophobia

At the outset the expectation was that claustrophobic patients would not be suitable for MRIdian treatment because of the length of time in the MR bore. However, in practice the radiographers have found that they can successfully treat them by using the in-built monitor screen, normally used by patients for the breath control function of automated beam gating. The screen is set up with landscape scenes, and the patient is guided with relaxation techniques to be able to lie calmly and watch the scenery.

"No matter how advanced this technology is we're patient-centred at the end of the day – I think we've done that really well"

Donna Hughes

The MRIdian service is designed around the experience so there are plenty of touchpoints and opportunities for patients to see how much care and consideration is given to their radiotherapy treatment. This includes meeting the clinicians on site during their treatment, which patients find very reassuring and is regularly cited in our patient satisfaction feedback. It is an extremely challenging time in our patients' lives and the treatment can be a daunting experience, so we try to make the service as 'special' as possible; we order in lunch and generally look after them. They also have access to our wellbeing services, such as Penny Brohn UK. We are finding that patients are prepared to travel a long way for this treatment and we do everything we can to help them with their accommodation and travel where needed.

"Another thing I've learnt is that the patient doesn't mind travelling. Most of my patients travel 120–130 miles to get to us. If you can provide the best treatment option, the patient will be willing to go anywhere and they always want the best treatment outcome."

Dr Prantik Das

"We get to hear a lot of feedback about how patients are doing after their treatment and it gives us a huge amount of satisfaction, both personally and professionally, to know how well they're doing and see the value of this treatment to them. A lot of our patients have limited treatment options and it's quite humbling to be a part of designing better care experiences that can achieve the best possible outcomes to patients."

Donna Hughes

A patient's experience

Doug was one of the first patients treated on the MRIdian with GenesisCare. He was referred to Dr Philip Camilleri with prostate disease and a PSA level 6.8, stage T2cN0M0 with a Gleason score 3+4 = 7 (grade group 2). Conventional radiotherapy in 20 sessions had been one of his treatment options, but when offered the opportunity to undergo treatment on the MRidian in five sessions he agreed.

Doug, our first patient

Although apprehensive, both he and is wife felt very reassured by the clinical teams involved and Doug was optimistic from the outset that treatment was going to be effective. His attitude was, 'let's get on with it!'

His advice to other people going into the machine is to relax and take things as they come. He said, "It is a procedure that is very, very technical, very accurate and one that will, with the right conditions, achieve the result that you're looking for. So relax, stay cool!"

After treatment Doug was soon able to resume his day-to-day life. He was particularly appreciative of the lack of intrusion the treatment had, commenting, "You don't feel you've had to donate a huge part of your life to getting over a cancer situation."

Prior to coming to GenesisCare, one of the options offered to Doug was to 'watch and wait'. This was one of the reasons for exploring other options.

"I can't express in words how life-changing it is to know that you're having a treatment, to see that your condition is improving."

When I think I could have been sitting around waiting on active surveillance for the next five years, waiting for something to go wrong, I can't say how wonderful it feels not to have that feeling.'

He added, "Having had the chance to experience this MRidian MR linac machine and to be taken backstage and look into the casing – being a mechanical engineer I am absolutely blown away by this piece of equipment."

Watch Doug's story here.

"It's very technical. Just relax and take things as they come"

Doug

At GenesisCare we are committed to adding to the body of evidence

MRIdian is new technology and although there is a relatively large body of data, it is mainly focused on individual centre experience rather than multi-centre, randomised trials that are needed to provide evidence of survival.

Collecting PROMs data for every patient

We have collected PROMs data for every patient that we have treated. This is designed around internationally validated tools, as well as bespoke, granular questions which were compiled with the support of our colleagues at VUMC in Amsterdam who have experience designing PROMs specifically for the MRIdian. Data are collected at baseline, during treatment, end of treatment, then at six weeks, and three, six and twelve months after treatment.

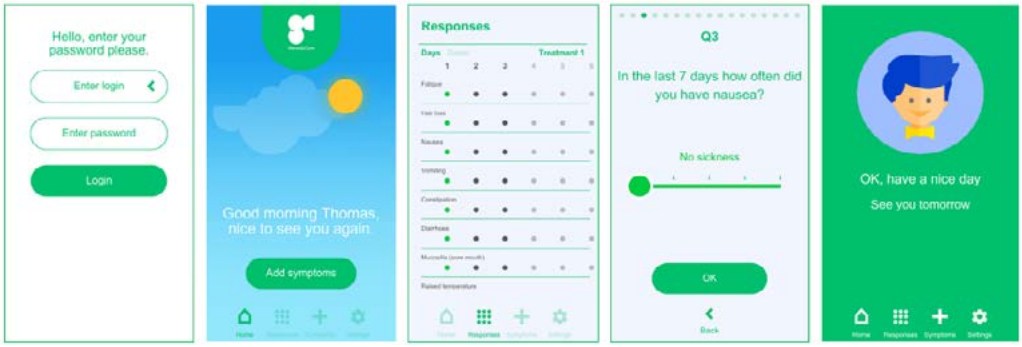


Fig 35: The PROMs app

PROMs feedback is administered using a purpose-built app, which patients find easy-to-use and improves the quality of our data collection. The radiographers are responsible for supporting patient compliance and this has so far proved a very effective method as they have a direct relationship with the patient.

As the first 50 patients reach three to four months post radiotherapy, we will start to look at some of the early indicators, such as acute toxicities, pain and quality of life.

There are indicators of reduced toxicity, with positive, anecdotal feedback from patients and clinicians.

"It's a really well tolerated treatment. We're seeing reduced toxicity because there is less dose into normal tissues. This does raise the possibility in the future of being able to increase the dose to tumours even further – and if we can increase the dose then that may impact positively on survival, but we don't have data to support that at the moment."

Dr Andy Gaya

Developing our unique partnership with the University of Oxford

GenesisCare has partnered with the University of Oxford to start to build a body of evidence that MRI-guided radiotherapy improves outcomes. This ten-year collaboration allows research access to the MRIdian with trials. 30 Oxford patients will be treated with this new technology this year, which has been enabled by a generous donation from the John Black Charitable Foundation.

"We're very excited to be offering access to patients across the country and are confident that having an increased number of successful patient] will demonstrate its merit to oncologists across the UK, and lead radiotherapy in the right direction"

Tim Maughan
Professor of Clinical Oncology, University of Oxford

UNIVERSITY OF OXFORD

This technology is going to make a difference for many patients

Increasing access

Already, this innovative technology has shown the opportunity to improve the way radiation is delivered. Our oncologists at GenesisCare in Oxford and many others around the world are treating patients differently than they ever thought they could. MRI-guided radiotherapy is going to become the standard of care for the majority of cancers – not all, but those where there is intra-fractional movement. It is efficient radiation, using fewer fractions and treating more patients – and as with all innovative technologies, the cost of the MR linacs used to deliver this will become more affordable.

"The link between Genesiscare and the University of Oxford provides a unique opportunity for NHS patients to participate in research studies on the MRIdian."

Dr Ami Sabharwal

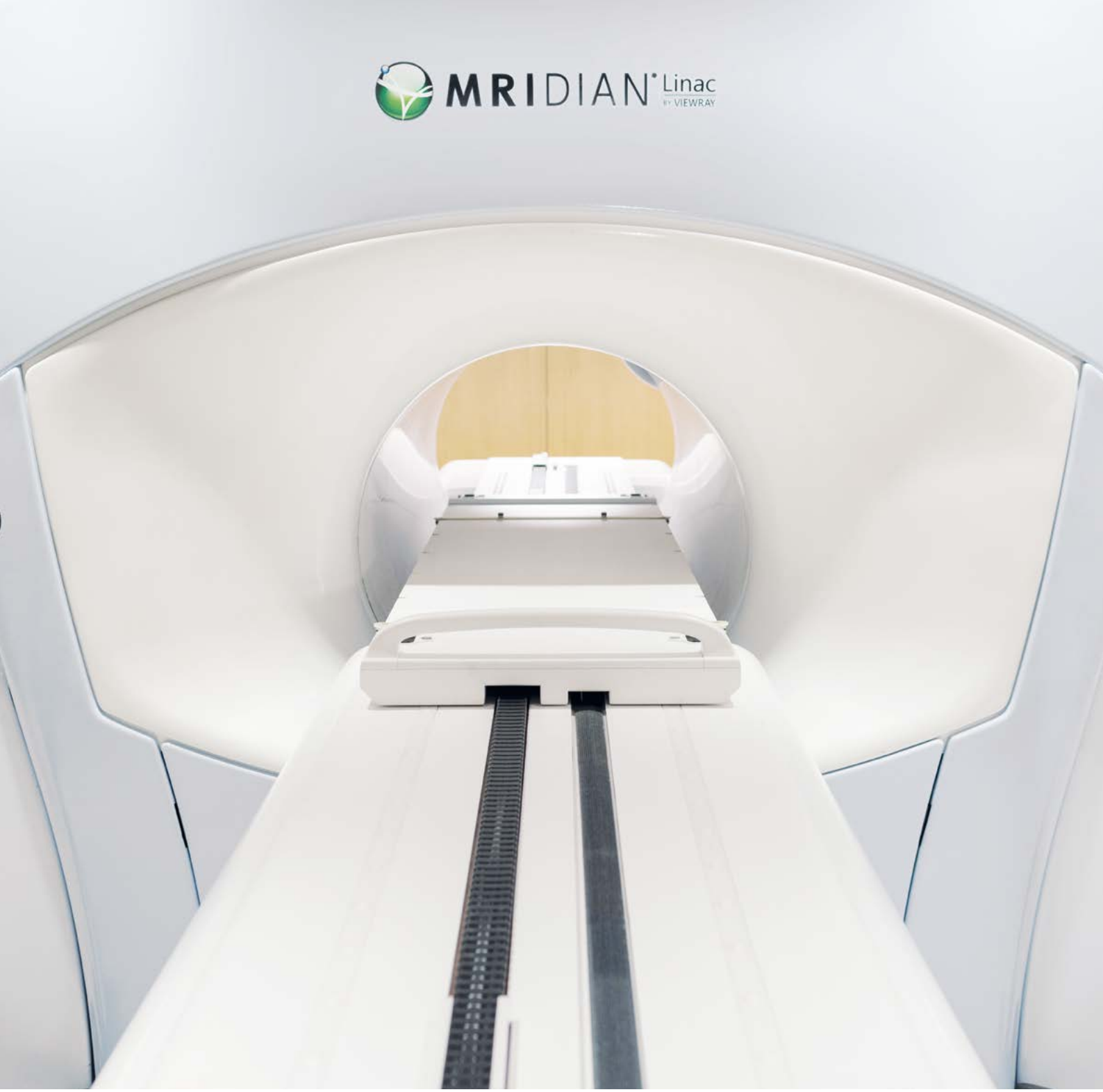
Education

One of the biggest challenges now is education. As one clinician said, "It is hard to overstate how, for some patients, it really does give you much greater confidence that you're giving the best treatment that is physically possible". We now want more doctors and healthcare providers to be able to see and use the MRIdian so that a greater number of patients will have access.

GenesisCare is now setting up a programme to invite NHS trusts to be part of our MR linac network. We will train their clinicians, physicists and dosimetrists so they will be ready when they get this technology.

Building evidence

Our commitment to developing the evidence base further will be achieved through the collaboration with the University of Oxford. This is a 10-year relationship and will involve numerous projects involving patients across the UK, including a clinical trial looking at expanding the use of MR linac into novel indications.



"As a team we've treated quite a few patients cautiously yet aggressively – it's opening a new horizon. We will soon be able to broaden the horizon further."

Dr Prantik Das

"Other centres are going to get MR linac and they're going to want to do this work. When they do, we'll be very happy to share what we've learned with them"

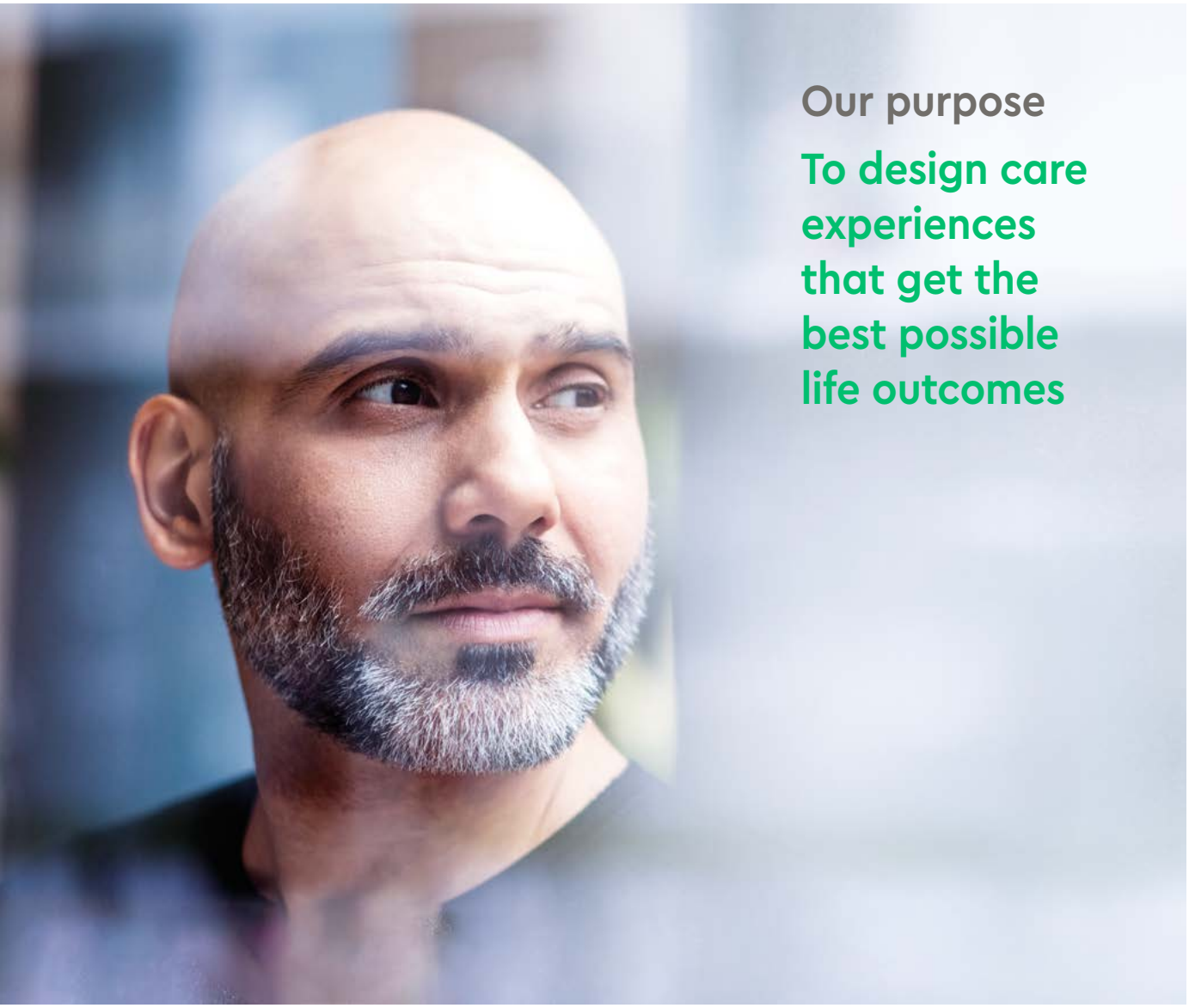
Dr James Good

To enquire about MRIdian please contact:

01865 237 700 | genesiscare.com/uk/mrl-hcp/

"Somebody has to go first and to innovate. We're fortunate enough to be able to be in a position to do that in GenesisCare"

Paul Gearing



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