MRI-guided stereotactic ablative radiotherapy for patients with localised pancreatic cancer
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Introduction

Radiotherapy is a vital component of cancer treatment – up to half of all people diagnosed with cancer receive it at some point during their illness. It works by focusing X-ray radiation onto the tumour. Because cancer is more sensitive to radiation than normal tissue, radiotherapy is highly effective in controlling tumour growth. Conventional radiotherapy often uses low doses of radiation to the tumour and surrounding tissue over several weeks. Stereotactic ablative radiotherapy (SABR) is a different form of treatment that uses higher doses of radiation, delivered just to the tumour, over three to five days. While it is not by itself a curative treatment for pancreatic cancer, SABR has been shown to be safe and effective in delaying or preventing localised areas of tumour growth.

The ability of SABR to control cancer growth with acceptable side effects depends on accurate visualisation of the tumour inside the body – especially because tumours in the pancreas move during breathing and are often surrounded by highly sensitive tissues such as the stomach, liver and duodenum. MRI-guided radiotherapy is the most advanced way of delivering SABR. This technique combines a radiotherapy machine with a magnetic resonance imaging (MRI) scanner and at GenesisCare is performed using the MRIdian system. MRIdian allows clinicians to see the tumour in real time, adjusting the treatment each day to ensure that it is as safe and effective as possible. Studies have shown that using MRI-guided radiotherapy we can deliver higher doses of radiation to a tumour than is possible with other radiotherapy machines, and that this may lead to improvements in survival.

Eligible patients who are undergoing care in the NHS can receive treatment on the MRIdian at GenesisCare in Oxford at no cost to the patient or the NHS. This has been made possible through charitable funding from the GenesisCare Foundation, Pancreatic Cancer Research Fund and ViewRay, the manufacturer of the MRIdian system. This initiative is also supported by a team of expert clinicians and the University of Oxford, who share a commitment to expanding the role of MRI-guided radiotherapy for pancreatic cancer through clinical trials.

The GenesisCare Foundation Compassionate Access Programme is now open to patients nationwide and is explained in more detail in this brochure.
Our aims

The GenesisCare Foundation
Compassionate Access Programme

- Provide access to MRI-guided SABR free of cost to patients with medically inoperable, locally advanced, borderline resectable, or locally recurrent pancreatic cancer, particularly where other treatments aren't available during the COVID-19 pandemic
- Build the evidence base for using MRI-guided SABR in the treatment of pancreatic cancer and to share this knowledge and expertise with the NHS oncology community
- Support the worldwide research community to find new and better ways to treat pancreatic cancer

You will find more resources here: genesiscare.com/uk/cap
Stages of Pancreatic cancer

As with all cancers, the treatment of pancreatic cancer is dependent on the stage, which means how far the cancer has grown and whether it has spread to other parts of the body.

Early stage cancers are often described as **resectable**, which means that they are potentially curable by surgically removing them. If the cancer can be removed from the pancreas and any surrounding organs, along with a clear margin of tissue around it to ensure that no cancer cells are left behind, then long-term survival may be achieved. Surgery is usually the best treatment for this stage of cancer but because of frailty or other illnesses, some people aren’t suitable. This is sometimes referred to as being **medically inoperable**.

People who undergo surgery for resectable pancreatic cancer usually receive post-operative (also called adjuvant) chemotherapy to reduce the risk of the cancer coming back. In some people, the cancer comes back in the area that was operated on, but not elsewhere in the body. This is called **locally recurrent pancreatic cancer** and it’s usually treated with chemotherapy or low-dose radiotherapy. When a cancer starts in the pancreas, it has often grown to a certain size before it is diagnosed, and has often grown around blood vessels next to it. While some tumours involving blood vessels are resectable, in other cases it can be hard to tell whether or not surgery will be successful in removing all of the cancer. This stage is referred to as **borderline resectable pancreatic cancer** and is often treated with chemotherapy first, and sometimes a five to six week course of radiotherapy, before surgery is attempted.

A cancer that is more advanced and definitely not resectable, but which has not spread to other organs such as the liver and lungs, is described as **locally advanced pancreatic cancer** (LAPC). This is usually treated with chemotherapy, and sometimes with a five to six week course of radiotherapy, or with low-dose radiotherapy to try to control symptoms such as pain or bleeding.

Pancreatic cancer that has spread beyond the pancreas and adjacent lymph nodes is called **metastatic pancreatic cancer**. This is treated with chemotherapy. In the unusual situation that there are only a small number of secondary tumours, SABR may also be used.
The role of radiotherapy in treating pancreatic cancer

Conventional radiotherapy

Conventional radiotherapy for pancreatic cancer aims to give a sufficient radiation dose to destroy cancer cells and a lower intensity to nearby healthy organs such as the stomach and duodenum (small intestine). Typically, this treatment involves a five to six week course of daily treatment sessions, in combination with chemotherapy. This combined treatment is called chemoradiation. Studies have shown that while this treatment helps control tumour growth, it does not have a significant impact on how long people live.

SABR allows radiation doses that can control tumour growth to be delivered in a much shorter time – just five days – and there is evidence that it may be more effective than chemoradiation in prolonging survival. For these reasons, SABR is an accepted standard of care in many parts of the world. At the time of writing, it is not provided by the NHS in England.

SABR with CT scanners

Conventional radiotherapy machines used for SABR have a built-in CT scanner that allows the treatment team to make sure the radiation is targeted to the right area. However, this technology does not allow really clear images to be taken meaning doctors have to limit the radiation dose to ensure no harm is done to normal tissues. By using MRI instead of CT guidance, MRIdian offers significant improvements in radiation targeting.
How MRIdian MRI guided radiotherapy can help

The combination of an MRI scanner with a radiotherapy machine, as well as other technical innovations that have been incorporated into MRIdian, offers three advantages for the delivery of safe and effective SABR.

MRIdian allows us to see the tumour with greater accuracy

Tumours in the abdomen are often in close proximity to normal tissues, such as the stomach or small bowel. It is often difficult to tell the difference between tumour and normal tissue using the CT imaging on a conventional radiotherapy machine. Because MRIdian has a highly sensitive MRI scanner built in, the ability to see the tumour during treatment is much greater. This gives us greater confidence in using SABR to target the tumour, while sparing normal tissue, and thereby reducing the chance of side effects.

MRIdian allows us to adapt to changes in organ position between treatment sessions

Tumours change, even over short periods of time. In addition to seeing the tumour and other tissues more clearly, MRIdian allows us to act on this by altering the way in which the radiotherapy is given to ensure each time you come for treatment, the best possible outcome is achieved. At each treatment session a new MRI is performed and the radiotherapy beams are adjusted to ensure that the tumour is being targeted and that healthy tissues are being spared. This is called adaptive radiotherapy and it is a unique advantage of MRI-guided SABR.

MRIdian allows us to target the tumour as it moves during treatment

MRIdian also has automated beam control, so if a tumour temporarily moves out of position – when the patient breathes, for example – the treatment will automatically pause. This ensures that the radiotherapy beams are precisely focused at the treatment target and helps to protect healthy tissues from damage. MRIdian is entirely non-invasive, with no additional procedure required to precisely locate the tumour.
Around 500 patients with inoperable pancreatic cancer have been treated on the MRIdian system worldwide. Several studies have shown that being able to deliver higher doses using the adaptive SABR process has resulted in lower side effects than when radiotherapy is delivered on conventional machines, despite higher radiation doses being given to the tumour. There is also some evidence that high dose SABR, made possible by MRIdian, improves survival.

GenesisCare and the University of Oxford have formed a ten-year partnership to develop the evidence base for this innovative radiotherapy technique. We believe that MRI-guided radiotherapy has the potential to improve treatment across a range of tumours, but that the evidence for its use in pancreatic cancer is particularly promising. The COVID-19 pandemic, which has restricted access to surgery and chemotherapy and makes chemoradiation less attractive due to the need to visit the hospital every day for five to six weeks, makes it even more important that all avenues to help people affected by pancreatic cancer are explored.

This initiative, the **GenesisCare Foundation Compassionate Access Programme**, is now open to patients nationwide. If you’re a patient currently undergoing treatment for pancreatic cancer in the NHS then this information is important to you.
Who is eligible for the GenesisCare Foundation Compassionate Access Programme?

To receive MRIdian MRI-guided SABR treatment there are various criteria you’ll need to meet and your clinician can help you decide if it’s right for you.

- You must have been diagnosed with pancreatic cancer that is currently medically inoperable, borderline resectable, locally advanced or locally recurrent, as described on page 5
- Your tumour mustn't be larger than 10cm in size
- You must be otherwise in reasonable health and able to have an MRI scan
- In addition, we’ll need up-to-date scans together with various assessments of your general health and also the health of organs such as your liver
- As each treatment can take over an hour, you must be comfortable lying within the MRIdian for that length of time

This treatment isn't suitable if you've had previous radiotherapy to the upper abdomen. It'll also not be beneficial if you've been told your cancer is metastatic (it has spread to other parts of your body). Your doctor will be able to explain this and discuss other options available to you.

MRIdian treatment for pancreatic cancer is recognised by all providers of private medical insurance. If you have private medical insurance, we request that you use this to fund your treatment, so that the limited funds available for our programme can be used to help NHS patients.

All UK citizens are eligible for the programme, but we regret that foreign nationals who are not eligible for NHS treatment are not eligible for the Compassionate Access Programme.
What happens next?

1. **Referral**
   Your own NHS clinician will need to complete our referral form. There are details at the end of this brochure.

2. **Decision**
   Our clinicians will discuss your referral at a team meeting. This team meets twice-weekly and we'll aim to respond to your referring clinician within 24 hours of the meeting.

3. **Appointment**
   If you're suitable for this treatment, you'll be asked to attend an appointment at a GenesisCare centre with one of our specialist teams of doctors (see right), each highly experienced in the use of MRIdian and SABR techniques for pancreatic cancer, gained from GenesisCare and the NHS.

**Planning appointment**
Prior to starting your treatment, you'll attend a planning appointment at our GenesisCare centre in Oxford. You'll be given specific information and there will be plenty of opportunity to ask questions, however, the following pages will give you an idea of what the treatment will involve.

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**Travel support**
Our partners, the Pancreatic Cancer Research Fund, are generously supporting patients who are accepted into the GenesisCare Foundation Compassionate Access Programme with the cost of travel or accommodation during their radiotherapy treatment. To find out more about this support, please telephone 01865 237 700

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**Oxford**
- Dr James Good
- Dr Andrew Gaya
- Prof Somnath Mukherjee

**Birmingham**
- Dr James Good

**Cambridge**
- Dr Alexander Martin

**Nottingham**
- Dr Luis Aznar-Garcia
What does MRIdian treatment involve?

Here is an outline of what to expect after your initial consultation and before, during and after your treatment. There are four stages to the process:

1. **Your planning appointment**
2. **Planning**
3. **Treatment**
4. **Follow-up**

Before your first appointment, your care team will call you to explain any preparation instructions in advance of your appointments and to answer any questions.

The ViewRay MRIdian platform is at the GenesisCare centre in Oxford. Transport and accommodation will be provided.
1. Planning appointment

The planning appointment will last two to three hours and will involve a magnetic resonance imaging (MRI) scan in the MRIdian and a computed tomography (CT) scan.

1. Your radiographer will explain the process and ask you to fill in a safety questionnaire

2. They’ll ask you to change into a gown and remove any objects which may contain metal such as jewellery, hearing aids, glasses or dentures

3. You may have a cannula (thin tube) inserted into your arm to inject a dye that improves the quality of your scans

4. You’ll be put in position for your MRI scan in the MRIdian. Your radiographer will make temporary markings on your skin and place soft pads (called coils) over your abdomen that help to produce high-quality images. They may ask you to drink some water just before your scan

5. The scan will take about 30 minutes. You can speak to your radiographer through an intercom system. They’ll give you breathing instructions to follow to help minimise movement of your internal anatomy. You can also listen to music using special earphones

6. When your MRI scan is complete, you’ll go to another room for your CT scan, which takes about 20 minutes. You’ll be placed in the same position as your MRI scan and given breathing instructions again

7. After your scans, you can go home. If you had a dye injected, you should drink plenty of water to flush it from your system

2. Planning

Over the following week, your consultant and care team will work together to create a MRIdian radiotherapy plan that is specific to you using advanced treatment planning technology.
3. Your treatment

Your treatment will be individualised to you so not all of the steps below will be applicable. Your MRIdian team will explain what will happen at each appointment.

You’ll need to fast for four hours before each session.

Prior to each treatment you’ll carry out many of the same steps as at your planning scans, such as removing accessories, changing clothes, getting into position and having the coils placed on your abdomen.

During each session, you’ll have a new MRI scan which will be compared with your planning scans. Your treatment plan will then be carefully adjusted and optimised to account for any movement of your tumour and internal organs.

Your treatment will take approximately 75 to 90 minutes. Your radiographer will ask you to follow breathing instructions for around 20 to 25 minutes during your treatment using a computer screen to help you. You can go straight home after each session. You’ll be given contact details for your care team so you can call if you have any questions.

4. Your follow-up

After your treatment course has finished, you’ll be referred back to your own doctor with all the information they need to plan any further treatment you may require.

**Seven to ten days later:** a member of your MRIdian care team will call to see how you’re feeling and answer any questions you may have.

**Four to six weeks later:** you’ll have a review with your GenesisCare consultant before being returned to the ongoing care of your referring clinician.

In the longer term, your MRIdian care team will continue to follow up on your recovery and wellbeing through appointments, phone calls and emails.

We’ll also ask you to provide feedback on your any side effects you’re experiencing by completing a questionnaire. This will be available to you in paper or as an app that can be downloaded on your phone.

We’ll also ask your referring NHS team to provide feedback on any scan results or side effects you may experience once you’ve returned to NHS care.
Side effects

Short-term
You may experience the following side effects during your treatment course, but they will usually disappear within three to four weeks. Your consultant will explain the side effects most relevant to you in detail before your treatment commences.

Common short-term side effects include:
- Fatigue
- Acid reflux
- Nausea
- Loss of appetite
- Temporary worsening of pre-existing symptoms

Uncommon short-term side effects include diarrhoea and constipation.

Long-term
These are uncommon, but may include:
- Stomach ulcers
- Stomach inflammation
- Duodenal (bowel) inflammation
- Rib fracture

Rare side effects include bowel or stomach perforation, bowel obstruction and kidney or liver failure. It’s important that you attend your follow-up appointments so we can identify and treat any problems as soon as possible.
How to apply

Your consultant at your treating NHS hospital will be able to refer you by requesting a referral form from our website. This can be found at genesiscare.com/uk/cap and we are available to answer any questions.

Please note that we can only accept referrals from an NHS consultant.
Our sponsors

The GenesisCare Foundation is an independent health promotion charity born from the philanthropic vision of GenesisCare. Its mission is to seek out and support life-changing improvements in cancer and cardiac care, in order to create profound impact at scale for both individuals and communities. It does so by investing in research that has the power to radically improve patient outcomes and by enabling access to innovative care. Chaired by Dan Collins, Founder and CEO of GenesisCare, the Board which governs the Foundation is comprised of experts in their fields who share a passion for philanthropy. Learn more at genesiscare.com/au/genesiscare-foundation

The GenesisCare Foundation Compassionate Access Programme has been made possible by donations from these organisations.

Pancreatic Cancer Research Fund is the only national charity dedicated exclusively to funding pancreatic cancer research. With this single-minded focus, its mission is to defeat pancreatic cancer by funding and promoting innovative, world-class research into the disease – research that will lead to the development of more effective detection, diagnosis and treatments and improved survival for patients.

ViewRay is re-envisioning radiation therapy to conquer cancer with the MRIdian® MR-Guided Radiation Therapy System. MRIdian allows clinicians to see as they treat, adjusting the beam to allow for movement and anatomical changes. The ability to target the tumor while sparing the healthy tissue brings a new level of control and confidence to stereotactic ablative radiotherapy. In routine clinical use throughout the world, MRIdian is revolutionising radiation oncology and changing the paradigm in patient care.
Research in the UK – our work

This is not a clinical research study and GenesisCare is treating all of our patients according to established protocols for the treatment of pancreatic cancer. GenesisCare and our colleagues at the University of Oxford ask all our patients if they will voluntarily consent to allow details of their treatment and response to be analysed by clinicians to understand the effectiveness of different approaches and how it can benefit other patients. You’ll also be invited to do this and it’ll include information about side effects and longer term response of your cancer, as well as feedback about your experience of treatment. As the role of MRI-guided radiotherapy grows, we believe that this will help improve the care of NHS patients in the future.

You can still have treatment under the GenesisCare Foundation Compassionate Access Programme even if you choose not to consent to this.

Oxford University is world-famous for research excellence, innovation, and home to some of the most talented people from across the globe. Its work helps the lives of millions, solving real-world problems through a huge network of partnerships and collaborations. The Oxford Institute for Radiation Oncology is one of the world’s leading centres for radiotherapy-related research and has established a 10-year partnership with GenesisCare, which enables the treatment of NHS patients on the ViewRay MRIdian® as a platform for state-of-the-art treatment and research.