Interventional Quarter ISSUE 3 - December 2010

Intervention IQ

Your portal to modern medicine

IR Without Borders

Global IR Statement

IR in Veterinary Medicine

Cancer Interventions

A New Era of Teamwork

Delivering Hope to Patients

www.intervention-iq.org

A Welcome from the Editor

Dear Readers,

At last, we are proud to bring you our follow-up Interventional Oncology issue! While part one provided an overview of cancer and its treatment generally, this issue will place the interventional procedures themselves under the microscope.

Although we received much positive feedback for part one, there is one alteration we would like to make. Unfortunately, some misunderstandings arose from our piece on the use of Yttrium-90 Radioembolisation, featured in Issue 1, *Understanding Cancer* on page 12. To clarify matters, we would like to amend our description of the procedure (see page 34), and apologise for any confusion caused. You can find more detailed information on the procedure in this issue, on pages 7 and 16.

But let us move forward – in order to provide you with the most up-to-date information, we sent our editorial team to the most important European meeting for interventional oncology, ECIO. The European Conference on Interventional Oncology is the premier meeting in Europe dealing with cancer interventions, and gave our team a chance to meet all the experts and hear their views on the past, present and future of the field. I am sure you'll be as excited as we are about the stellar line-up of researchers featured in this issue of IQ.

Interventional oncology represents a major opportunity for both interventionists and for all those who wish to provide patients with the most tailored oncology treatment possible. We are especially grateful to our non-IR contributors, whether radiologist, surgeon or oncologist, for taking an energetic role in furthering our shared goal of establishing a comprehensive multidisciplinary approach to patient care.

As usual, a change of pace is offered by our supporting content, among which we are proud to count an exclusive interview with one of the greatest living IR pioneers, Josef Rösch. Be sure to read his reminisces of *the Early Days of IR* on our back page.

We wish you pleasant reading, and, as always,
look forward to your feedback!

Jim A. Reekers
Editor-in-Chief

General Information

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An invitation to our readers

IQ is your magazine, and we would welcome your views and your news. Readers who wish to comment on any of the issues raised (or who would like to raise any of their own) are most welcome to submit letters to the Editor. Likewise, if you have any promotions, awards, honorary lectures or other tit-bits you'd like to share with the interventional community, please send them to us by post or by email.

We look forward to hearing from you!
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Contents

Cancer
Interventions

Cancer is a disease group that is estimated to affect one in three of us during our lifetime[1]. Cancer has always been with us - it is a disruption at cellular level that can invade other cells, and is not just limited to humans - all living creatures can be affected by cancer, even plants. However, its prevalence has been increasing steadily for the last 150 years. This can be explained by two major phenomena: the success of medical science in prolonging our life expectancy and minimising the impact of previously fatal diseases such as pneumonia; and our ever-increasing exposure to carcinogens - substances such as tobacco smoke, industrial fumes and food additives, which can cause DNA mutations or speed up the rate of cell division.

This means that medicine is, by necessity, becoming ever more focused on treating cancers, but as it is a diverse class of diseases, a diverse range of treatments is needed. Interventional radiology (IR) has long been offering cancer patients palliative treatment for the complications of their disease, but in the last decade or so, it has leapt forward to take a more active role in oncology, giving birth to a new subspecialty: ***Interventional Oncology***.

Advances in cancer care

These advances join the many other medical innovations that are tackling both the root causes and effects of cancer. Advances in diagnostics are not only helping catch cancers earlier; they are also allowing doctors to learn more about the properties of the cancer in question. In knowing more about the specific make-up of a cancer, doctors are able to choose therapies that will be most effective. And there is a lot to choose from: new drugs are being developed that can fight cancers more effectively; gene therapy seeks to alter the DNA defects that trigger the cancer; targeted therapy can hone in on specific molecular structures; and combinations of all the above are being experimented with.

> IR has long been offering cancer patients palliative treatment... but in the last decade, it has... taken a more active role in oncology

Development of IR

IR has a vital role to play in all this. It can help both deliver and activate these drugs and genetic and molecular treatments. It can also play a separate, though supporting, role - actively treating the tumours themselves, either to shrink or to kill them. There are many different ways that IR can achieve this (see pages 6-11). It also continues to provide patients with the palliative care it has offered for decades, helping control the symptoms and complications of cancer, such as superior vena cava syndrome.

Multidisciplinary approach

This broad range of medical, surgical and radiological options allows doctors to combine therapies to overwhelm cancer cells and bring relief to patients. Any successful general will tell you that you do not try to storm the city through the front gate alone - likewise, by mounting a multi-fronted attack on cancer, the potential for success is vastly increased. Multidisciplinary clinics are fast becoming the new model for cancer treatment, as specialists acknowledge that their treatments can often be enhanced by their colleagues.

> By mounting a multi-fronted attack on cancer, the potential for success is vastly increased

Patient selection

However, these treatments are not a golden bullet, and what will work for one patient may not work for another. Accordingly, proper patient selection protocols must be followed before offering a patient any treatment. This is another reason for the rise of the multidisciplinary clinic. Surgeons will recognise if a patient is unresectable, but they will not necessarily know if the oncologist or IR will obtain the better outcome. With all disciplines working in close consultation, patients can be rapidly assessed and given the safest and most effective form of therapy available for their specific cancer type.

The therapeutic possibilities are manifold, and offer real hope in a medical realm that was previously characterised by stoicism at best, and pessimism at worst. It is an exciting step forward - for IRs, for the medical field as a whole, and for the one in three of us who will pull the short straw.

Please refer to Interventional Quarter Issue 1, March 2010 or www.intervention-iq.org for:

- *basic facts behind the condition*
- *cancer types and their possible treatments*
- *more interviews with leaders in the field*

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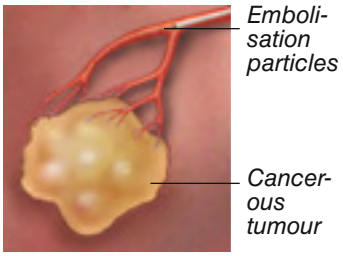
1 *www.macmillan.org.uk*

IR treatments in detail

Bland Embolisation

Dr. Yasuaki Arai (Tokyo, JP)



Embolisation blocks the blood supply to the tumour. This is done by inserting a catheter into the femoral artery through a small nick in the groin, and feeding it under image-guidance to the problem area. The catheter then delivers tiny clotting agents (plastic particles, coils, gelfoam, etc.) directly to the area to stop the blood flow to a tumour, causing it to eventually shrivel and die. This is carried out under local anaesthesia.

"Embolisation is one of the most powerful treatment modalities and is very effective in most cases of cancer treatment.
"It is also a highly cost-effective procedure compared with the more expensive treatment modalities, such as molecular-targeted agents (sorafenib, bevacizumab). Even taking into account the microcatheters and beads that can be used for embolic procedures, the total cost is still much lower in comparison to newer pharmaceutical agents.
"I think this branch of embolic therapies will have a huge clinical impact, especially in countries that cannot afford to buy expensive targeted drugs for their cancer patients. Another very important point is quality of life and very good results have been recorded for pain control. I think that this is another new developing treatment."

Dr. Arai leads a Japanese trial group, the Japanese InterVentional Radiology in Oncology Study Group: jivrosg.umin.jp/e_index.htm

Transarterial Chemoembolisation (TACE)

Prof. Philippe Pereira (Heilbronn, DE)

© *Biocompatibles*

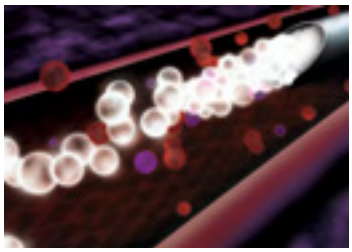
TACE uses the same process as bland embolisation, but the materials used are different.
The clotting agents are dosed with cancer-fighting drugs. As the drugs are delivered locally, rather than system-wide, doses up to 200 times stronger than conventional chemotherapy can be used. These can remain active in the tumour for a month, treating the tumour and blocking blood supply simultaneously.

"We have been using chemoembolisation for 27 years but the breakthrough has really come in the last 10 years with the emergence of new drugs and new embolic materials which allow more precise embolisation and more concentrated drug dosages.
"The advantages of tumour embolisation are obvious. It allows very precise targeting of the lesion, and you do not have a systemic delivery of the drug, so you have less toxicity.
"I believe the future in the field of oncology is combined therapies - combining TACE with anti-angiogenic therapy, adjuvant chemotherapy, or thermal ablation, thereby increasing the effects of embolisation. As we only treat the tumour itself and not the underlying disease, working together with our oncological colleagues is essential to provide patients with optimal care, which is why the multidisciplinary model is on the rise."

Dr. Jim Caridi (Gainesville, FL, US)

"A great step forward in the last 5 years is what is known in Europe as DC beads (doxorubicin compatible), which were approved in the US without doxorubicin, so they are called LC beads - low compression beads. These are mostly used for liver cancer, but the other application being tried is the treatment of liver metastases from colorectal cancer, where we add a different drug, irinotecan. Although the complications are not high with traditional TACE, there is a small percentage of patients that will experience side-effects such as alopecia (hair loss) or bone marrow suppression. This is almost non-existent with the beads which have less liver toxicity compared with traditional TACE, reducing the possibility of irritating the liver. But a key point of the beads is the level of standardisation it can help bring to the technique."

Radioembolisation



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Dr. Tobias Jakobs (Munich, DE)

"Radioembolisation is a loco-regional cancer treatment of primary and secondary liver tumours, where microspheres that are labelled with a radioactive isotope are injected via a transarterial catheter into the tumour-bearing liver areas. Patients should not have an elevated bilirubin level, so some laboratory tests are needed to rule out contra-indications. Similarly, cirrhosis should not be too advanced, so usually in primary liver cancer, you should only treat patients with a Child-Pugh A, or with a good Child B liver cirrhosis.

"We now see that referring physicians are considering IR earlier in treatment discussions. With the recent developments of the technique itself, we are now performing radiation segmentectomy on patients who have very limited tumour burden in the liver. We are also seeing an increasing number of patients who have tumours only in the right or left liver lobe, carrying out more and more lobar treatment, which is usually even better tolerated by the patient with fewer side-effects.

"By having access to state-of-the-art equipment like cone-beam CT and high-end angiography units, we can limit the occurrence of complications to a very low level, which ultimately increases our confidence and the patient's safety."

For more information, please refer to page 16.

Intra-arterial Chemotherapy

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Prof. Thomas Vogl (Frankfurt, DE)

In intra-arterial chemotherapy, high-dose chemotherapy is locally applied directly into the tumour-feeding arteries. It uses only 60% of the drugs normally prescribed, yet the results are as good as or better than systemic treatment and it has fewer side-effects. At present, it is only used as a last resort, but promising results in a wide range of tumours may make it a primary treatment in the near future.

"We have 3 main goals in using this therapy for primary and secondary lung tumours: firstly, we believe the therapy obtains good results in patients who have previously been treated with systemic chemotherapy or radiotherapy and are showing a relapse. Secondly, our data on more than 200 patients show that we are able to achieve a further tumour control in about 60% of patients, thus allowing us to improve the local control rate and the symptoms for the patients, and thirdly, we are on our way to demonstrating that survival can be improved.

"Good cooperation between medical oncologists, radio-oncologists and IRs is essential if dosages are to be calculated and delivered accurately, offering the patient optimum treatment.

"From our observations of modern oncological centres and oncology conferences, there is a strong tendency towards multimodality treatment and I think that patients in a recurrent or relapse situation will demand more of these applications."

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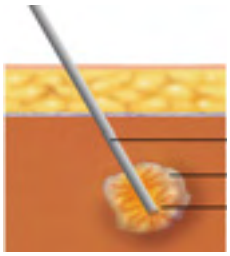
Radiofrequency Ablation (RFA)

Dr. Thierry de Baère (Villejuif, FR)



RFA probe cancerous tumour radiofrequency heat

RFA is a minimally invasive treatment in which tumours are killed using high frequency alternating currents which produce heat. The treatment has been proven to be safe and effective and can be repeatedly used on both primary and metastatic tumours. The RFA procedure consists of a needle-like RFA probe being inserted into the tumour, where the intense heat it produces ablates the tumour. The treatment targets the tumour mainly, with minimal damage to the surrounding healthy tissue.

"Ablation in IR terms means to destroy or burn the tumour, leaving in place granulation tissue to be cleared by the immune system. Ablation started in around 1996 with RFA, which is still the most common thermal method by far. However, this situation may well change in 5 years as we are now seeing the emergence of microwave and cryoablation, which allow the targeting of larger tumours, and more reproducible ablations.
"Since its beginnings, we have witnessed major improvements in the technique, the devices and image-guidance. In the early days, ablation techniques were only performed on non-surgical candidates, however their efficacy in treating small tumours is now on par with surgical resection. This was supported by two renowned surgeons and guest speakers at the European Conference on Interventional Oncology (ECIO 2010), Doctors Vincenzo Mazzaferro and Pietro Majno, who both asserted that for a small primary liver tumour, ablation and resection are comparable.
So, we have moved from a world where ablation was only for patients that were not able to have surgery, to a world where they prefer RFA for small tumours - it is most probably the low rate of complications that is making the techniques more and more popular."

Cryoablation

Dr. David Breen (Southampton, UK)

Cryoablation is the use of extreme cold to destroy diseased tissue such as tumours. In cryoablation, probes are inserted into the tumour through a small nick in the patient's skin and an extremely cold gas then chills the probes (to approximately -140°C or less) which then goes on to freeze the cancer target to -30°C or less. The process of repeatedly freezing and thawing the tumour kills the cancerous cells and a safety margin around the tumour, without affecting the surrounding healthy tissue. Following the procedure, the dead tissue scars down and is cleared by the patient's immune system. There is some evidence to show that the process also stimulates the immune system to attack any remaining, remote cancer cells.

"One of the main advantages of cryoablation is that you can see the ice ball evolving very easily on CT and MR, which allows for very accurate treatment dosimetry and procedure control. This is an immense step forward in delivering accurate and complete ablation of small (<5 cm) tumours.
"There is also clear evidence to show that a cold-based therapy is less painful and there are fewer analgesic requirements. Regarding the other areas of interest, it causes a different type of disruptive tumour cell death, and some work suggests it may expose tumour antigens, aiding the body in its response against that tumour if present at other sites.
"Very good long-term data is accruing in kidney cancer, and in prostate and palliative bone applications. We have also used it in focal adrenal disease.
"I have been dealing with RF ablation for many years, but I can see a shift towards microwave and cryoablation. These ablation techniques are in the ascendant and clearly have individual merits in different cancer applications."

Microwave Ablation (MWA)

© iconspro

Dr. Laura Crocetti (Pisa, IT)

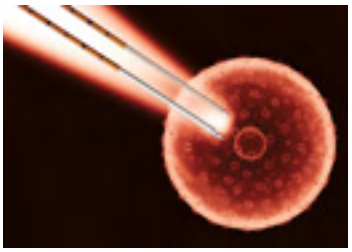
MWA is the most recent development in the field of tumour ablation. The treatment, which uses electromagnetic microwaves to destroy cancerous cells, is, once again, highly precise and does not cause damage to healthy surrounding tissue. Other advantages of MWA include the fact that multiple lesions can be treated simultaneously and larger tumours can also be treated. In MWA, a thin microwave antenna is placed directly into the tumour under image-guidance (typically ultrasound). A microwave generator then emits an electromagnetic wave through the antenna. The electromagnetic microwaves cause the water molecules in the tumour cells to spin and create intense heat, which in turn kills the cancerous cells.

"The main advantages of microwave technology include consistently higher intratumoural temperatures, larger tumour ablation volumes, faster ablation times and, consequently, an improved convection profile. Because MWA does not rely on an electrical circuit like RFA, multiple applicators can be applied simultaneously, and placement of grounding pads on patients' thighs is not required.

"MW has been used clinically in Japan since the early 2000s, but recent advances in microwave engineering have allowed for new microwave systems with larger, more controlled ablation zones, overcoming the limitation of the small volume of coagulation that was obtained with probes used in early experiences.

"Microwave technology has evolved significantly since its recent beginnings, creating a need to produce clinical data to confirm the efficacy and safety profile of MWA. The goal would be to enrich the treatment's algorithms with a new option rather than completely substitute the present ones."

Irreversible Electroporation (IRE)



Dr. Raj Narayanan (Miami, FL, US)

Irreversible electroporation (IRE) is a novel interventional treatment for the ablation of soft tissue cancers. Electrical pulses are applied across cancerous cells, thus irreversibly damaging the membranes of the cells and creating small openings. This increased porosity destroys the cell's ability to maintain its inner environment (homeostasis), and they die as a result. The non-thermal nature of IRE means that it can be used close to blood vessels and nerves. It is also highly precise and healthy surrounding tissues are left undamaged. A device which is currently being used in America for the safe and effective IRE ablation of soft tissue cells is the Nanoknife from Angiodynamics (see page 28).

"IRE has FDA approval for use in soft tissues in the States, and we started with our programme in January 2010. To date, we have performed about 45 treatments in 30 patients, mostly in the liver. So far, over the last nearly 6 months now, we have not seen any recurrence in the treatment zone - it has remained completely non-advancing, which is very encouraging.

"It is very precise and definitely safe; we use it in lesions located close to other organs, and so far have not experienced any major issues.

"The other great advantage is being able to treat tumours close to vessels percutaneously, which we could not do with radiofrequency ablation (RFA). This is because the collagen that provides the support for vessels is unaffected, leaving vessels in the treatment zone and bile ducts intact."

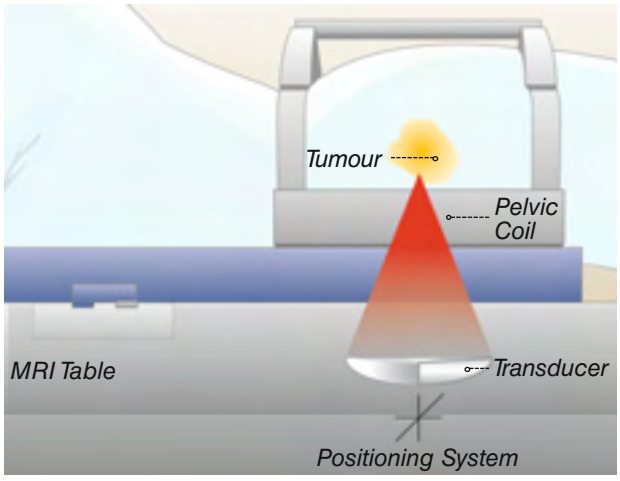
IR treatments in brief

Interstitial laser therapy

Laser interstitial thermal therapy (LITT), or **laser-induced interstitial thermotherapy (LIIT)**
Laser ablation is used to ablate primary and secondary lung tumours. Local anaesthetic is first applied around the tumour. A hollow probe is inserted into the tumour using image-guidance, and a laser fibre is placed within it. A multi-sensor thermal needle is inserted through another site to monitor the heat generated. Energy is transmitted into the tumour, destroying the cells. A major advantage of laser ablation is the possibility of using it under MR-guidance, which would expose patients to less ionising radiation throughout their therapy. Trials are currently being run on bladder, prostate, liver and breast tumours.

High-intensity focused ultrasound (HIFU)

HIFU has several clinical applications; one being a heat-activator for cytostatic drugs (see overleaf, "Drugs"). Currently, the main application is as a thermal ablation modality. While ultrasound energy can pass through soft tissues without causing any damage, if this energy is focused, heat can be generated on a very small area to destroy tissue. The ultrasound beam will pass harmlessly through other non-target structures, making complications extremely unlikely, although HIFU should not be used on lesions that border on other sensitive organs, such as the intestine or bowel. The procedure is planned and guided by another imaging modality, most commonly MRI, but also ultrasound. This allows the tumour's outline to be traced very precisely. MRI's thermal feedback allows the physician to judge the heat delivery in real time. It is currently being used worldwide to treat uterine fibroids, and in Europe to treat painful bone metastases. Clinical trials are underway on breast, brain, prostate, liver, kidney and pancreatic tumours.



Chemical ablation

One of the earliest forms of ablation was chemical ablation, where substances such as ethanol were directly injected into the tumour to cause cell death (percutaneous ethanol injection or PEI). Multiple sessions were needed to obtain complete tumour necrosis. Although no longer widespread, it is still used in some centres for treating HCC and thyroid lesions, and technical advances such as the QuadaFuse injection overcome the traditional limitation of poor ethanol diffusion due to intra-tumoural septa. Other applications include combining it with RFA to enhance efficacy.

Light-activated therapy

As early as 2000, drugs were developed which could be activated by light. These drugs would be delivered systemically, but tended to accumulate slightly in the tumours. They could then be activated in the desired regions by shining a non-heating laser light onto the tumour, releasing a toxic form of oxygen that had a bleach-like effect. The poor penetration of the light, however, restricted its application to superficial skin tumours. By mounting light-emitting diodes at the end of a flexible guidewire and using image-guidance, IRs are able to insert the light source deeper within the body, using only mild sedation. Its kill-zone of 4.5x2.5cm can be enlarged by using multiple catheters. As it is a non-thermal procedure, there is no heat-sink effect, and no injury of vascular structures of adjacent organs. Light-activation mechanisms are also being adapted for gene therapy (see overleaf).

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Drugs

There are many advances being made in drug technologies, namely biological anticancer agents that specifically target a tumour growth, or angiogenesis regulation pathways such as VEGF or EGFR. IR can help in delivering some of these agents to particular regions, mainly by intra-arterial catheter delivery. As some drugs are being developed that are heat-activated (or at least more efficacious under heat), IR is needed to provide the activation mechanism. Heat can be used in some cases to activate the drugs themselves; in some, to rupture the "skin" they are carried in. In one variation, the drugs can be tracked under image-guidance, and heat (RF, HIFU, MW, etc.) can be applied when they reach the target. In another variation, the drugs themselves can be designed to have uptake in the specific tumour tissue, and do not need to be tracked by image-guidance.

© irin-k

Magnetic chemotherapy

Magnetic chemotherapy is still in development. Nanomagnets (nanometre = the distance a fingernail grows in one second) are stem cells tagged with microscopic particles containing iron. Scientists have succeeded in steering these, using an external magnetic field and image-guidance, to target some conditions in rats. As nanoparticles are already approved for use in humans by the FDA (US), human trials could begin within three to five years. By using this technique to tag antibodies or viruses, cancerous tissue could viably be targeted. This procedure can be used to target, and with MRI, to observe cell behaviour.

Gene therapy

There are numerous research projects in progress to find ways to use genetic alteration to fight cancer. One method involves activating the patient's own immune system (a de facto vaccine); another, replacing faulty genes with healthy ones; a third, by genetically making cancer cells more susceptible to chemotherapy agents; or by combining antibodies and cytotoxic drugs within a liposome, so it targets the cancer specifically. There are many possibilities, and some projects are showing excellent potential. IR is expected to play an important part in delivering these treatments.

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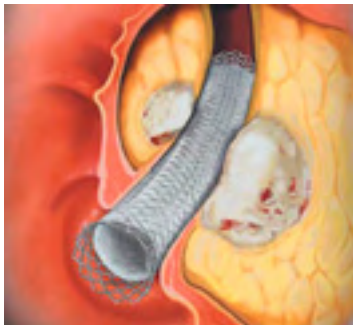
Stereotactic body radiation therapy (SBRT)

SBRT is a new method of delivering radiotherapy that requires fewer applications than traditional radiotherapy, and has fewer side-effects for the patient. Multiple radiation beams are used to precisely target the tumour, by means of many different angles. A specially designed co-ordinate-system is used to exactly localise the tumour. As many organs continually move due to breathing, etc., the treatment is coordinated by frameless stereotaxy (see page 13). The radiotherapists who perform this procedure require the help of IRs to place fiducials (tracking landmarks, often metal particles) in the patient's tumour under image-guidance. Once the fiducials are in place, the tumour can be more accurately targeted during the procedure.

Stenting and palliative treatment

Tumours can sometimes affect the ducts and vessels of the body, obstructing and sometimes blocking off the food, fluids and waste products that flow through them. In such cases, stents can be used palliatively as a means of relieving the patient of the negative symptoms that can arise, thus improving their quality of life. Palliative treatment for Superior Vena Cava Syndrome (SVCS) is a prime example. SVCS is a disease in which the blood flow through the superior vena cava becomes obstructed, usually by a cancerous growth. A stent is placed in the narrowed part of the SVC, enabling blood to flow more freely, alleviating the patient's symptoms of venous distension, facial swelling, headaches and shortness of breath. Stents can also be used to hold open obstructions of the oesophagus, bronchus and colorectal tract.



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Advances in imaging

IQ is proud to present the *Imaging Panel*, consisting of prominent figures in diagnostic and interventional radiology. Here, the experts discuss the latest innovations in imaging and the major role they play in advancing IR.

With these and other advances, IR now has more options for planning, navigation and follow-up than ever before, allowing for even more accurate and effective treatments and offering the patient even better outcomes.

To begin, Prof. Szczerbo-Trojanowska, could you please explain the significance of imaging before, during and after an IR procedure?
Imaging is absolutely crucial for image-guided interventions, and we have many new possibilities to perform good pre-procedural imaging. Localising and evaluating the lesion with high precision is important: good, detailed images allow us to choose the most suitable treatment, to thoroughly plan the procedure strategy and to select the most suitable devices and the optimal trajectory to reach the lesion.
During the procedure itself, we rely heavily on the ability to visualise the lesion, tools and progress of the intervention, and we now have a number of imaging options to help guide instruments and devices.
Follow-up is playing an increasingly important role in IR too. Nowadays, with so many procedural developments being introduced, it is of utmost importance to accurately evaluate the effectiveness of treatment. It is also vital to detect recurrence of the disease as early as possible. Advances in imaging give us more refined and specific ways to visualise all these important elements.

Contrast-Enhanced Ultrasound (CEUS)

One such advance is the progression of ultrasound. In recent years, contrast media have been developed which enhance the reflection of sound waves, giving a sharper image. Prof. Szczerbo-Trojanowska, what are the main advantages of the recently developed Contrast-enhanced ultrasound?
Contrast-enhanced ultrasound provides new, valid information on the intra-tumoural vascularity and blood flow, comparable to the information obtained by Computer Tomography (CT) and dynamic Magnetic Resonance Imaging (MRI). But there are also many other advantages, such as no exposure to radiation, and the absence of nephrotoxic contrast agents.

Is it too early to talk of a clinical impact?
Although a recent development, ultrasound (US) contrast media are already having a huge clinical impact. Besides providing additional information to US investigations, they play a particularly significant role in follow-up. For instance, after aortic stent-graft implantation, patients are routinely screened at 1, 6 and 12-months, subjecting them to CT three times in one year and accordingly, to radiation and contrast medium injections.
However, in our department we introduced a new scheme of follow-up using contrast-enhanced ultrasound. Our first results are very good, as we have never detected any endoleak in CT which was not detected in ultrasound with contrast. Now the patients are followed with contrast US and receive CT only after 1 year, which lowers costs and reduces radiation harm to the patient.

Diffusion CT/MR - Perfusion CT/MR

The issue of patient safety is a driving force of these new developments. Dr. Della Pina, it is certainly in the best interests of the patient that good collaboration exists among physicians. Is it important for this to exist between diagnostic and interventional radiologists too?
Yes, there should be a close partnership; it is essential for an IR to know if treatment is successful, and this is where diagnostic radiologists can help their interventional colleagues. We now have some new sequences with CT and MR, such as diffusion and perfusion, which can differentiate between the necrotic and valuable parts of the tumour, and it is essential for an IR to know this. We are currently investigating diffusion MR following RF ablation and chemoembolisation.

A technique which demonstrates a perfect marriage of diagnostic and interventional radiology. Could you perhaps tell us a little more about diffusion MR?
Diffusion MR is a sequence in which we do not use MR contrast agents - a baseline sequence that takes 20 seconds to perform. On a workstation, we calculate a coefficient (a number). This number is called the “apparent diffusion coefficient” and gives an idea of the movement of water molecules in the cell, in the nodule and in the tumour in general. The movement of water molecules can differentiate benign and malignant lesions since the diffusion of water in malignant tissue is restricted by necrosis, fibrosis, etc.

So, how does perfusion compare to diffusion? What are the main differences for the follow-up imaging in interventional radiology?
Perfusion is a little different because a contrast agent is used, and we can calculate the distribution of the contrast agent inside the nodule. But this sequence is still under validation; diffusion, on the other hand, is very easy to do, and is now routine in the centres where IR is performed. Perfusion is less used in MR due to lengthy procedure times, software problems and intricacy of the sequence. Diffusion is easier and quicker, which is preferable to both patient and clinician.

3D Segmentation

Dr. Cioni, you work alongside Dr. Della Pina in the Division of Diagnostic Imaging and Interventions, Department of Hepatology and Liver Transplantation, University of Pisa - what kind of advanced imaging technology do you find particularly interesting at the moment?

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University of Pisa
Italy

Well, for example, an advanced semi-automatic segmentation volume method (SVM, INTIO Inc.) has been recently developed and is currently under investigation in our centre. SVM involves placing a seed (or multiple seeds) on the centre of the liver tumour. A region is then selected to calculate the density of the normal hepatic tissue. The segmentation is based on a 3D active contour approach as proposed by Osher and Sethian in 1988. SVM allows reliable segmentation of liver tumours, suitable for clinical application in treatment planning and response assessment. These advances help to obtain a more complete and radical therapy.

In what area is this showing great promise?
In the liver, in particular, tumour segmentation is a challenging task due to a large variability in appearance, density, shape, and size of the lesions. However, volumetric CT approaches such as 3D segmentation of tumours, improve treatment planning and response assessment. Manual segmentation is time-consuming and error-prone, but automatic and semi-automatic methods are already showing the potential to provide fast, objective and accurate tumour segmentation.

Robotics

Although the application of automated systems to ensure pinpoint accuracy is not a new concept, it is certainly an exciting field which promises to revolutionise IR. Prof. Szczerbo-Trojanowska, what can we expect to see in the future?
Further progress and refinements in accuracy of some of the IR procedures will come from the introduction of automated navigation and robotisation. A needle or other instrument will be directed and advanced by robots which will secure the highest possible accuracy and precision. This has already been experimentally introduced in brain surgery, surgery and radiation oncology, so the use of robots and automated procedures in IR is just a matter of time. Indeed, devices (PIGA CT, Perfint Healthcare Ltd.) have already been developed which allow precise, automated needle placement in the target identified in CT images. Automated navigation poses considerable difficulties in moving organs, such as lungs, heart and abdomen, but continuous imaging with US or x-ray correcting pre-procedural MR and CT images already offer solutions to this problem.

Stereotaxy

The development of frameless stereotaxy is one such solution. Prof. Bale, this is your particular area of expertise; perhaps you could tell us when the technique began and how has it developed?
Since 1900, neurosurgeons have been mounting stereotactic frames to the skull and using a 3D coordinate system to precisely target lesions with submillimetric precision. Stereotaxy means "navigate in 3D space", in a Cartesian coordinate system. The problem is, you cannot fix a stereotactic frame on an organ such as the liver of course, the liver moves up and down, so it was necessary to develop a frameless stereotactic navigation system.

This sounds incredibly futuristic; what does this involve and which method is employed to destroy the tumour?
This requires you to register the liver to a 3D space, and correlate the virtual volume to the real patient - bringing together the virtual patient with the real patient. You can do this by using landmarks (fiducials) somewhere on the skin or anatomic landmarks, and using respiratory motion control. You then plan the virtual data set in the CT, you plan your pathway from entrance point to target point and with the aiming device and the probe, you align the virtual path with the real instrument. Ablation can then be used to destroy the tumour.

How established is the procedure?
This is in trial phase in Innsbruck. We started in 2001, and have now treated up to 800 tumours in 290 patients, with a local recurrence rate of 6.3%. Most people only ablate tumours less than 3 cm, but our aggressive approach has enabled us to treat tumours up to 15 cm with good results. The difference is that we place on average 8 needles; all others place 1-3 maximum. My aim is to completely destroy every single cell in this tumour.
Our data says that with Stereotactic Radiofrequency Ablation (SRFA), we can achieve the same local recurrence rate with as resections. We have 2-3 times less morbidity and 2-3 times less mortality than resection, and the same local recurrence rate and similar long-term survival rates - ours being only slightly higher, but then we have only treated non-resectable patients. So we are not comparing apples with oranges, but apples with rotten apples. We treat the rotten apples, with positive results.

Why IR is gaining ground

Due to the evolution of both IR itself and multidisciplinary care, IR is steadily making an increasingly bigger impact in the field of cancer management. Being able to perform a procedure is not enough - structures must be in place that allow suitable patients to receive these treatments.

Evidence-based medicine
IRs are beginning to help build these structures, and with the financial support of their industry colleagues, multiple trials are underway that will evaluate the best clinical indications for these procedures, and when in the treatment plan they should be considered. As newly developed techniques, IR procedures have been traditionally reserved for "no hope" cases, where all other pharmaceutical, surgical and radiation therapy treatments were unsuccessful. With good clinical data under their belts, IR is beginning to be considered for early stage treatment, and in many institutes and guidelines, procedures such as radiofrequency ablation are recognised as providing certain advantages over other potential therapies. Further trials are underway, and may demonstrate that techniques such as chemoembolisation or irreversible electroporation are ideally suited to certain clinical criteria, either alone or in combination with other therapies.

> With good clinical data under their belts, IR is beginning to be considered for early stage treatment

Research is also being done into combined therapies, whether they be combinations of established therapies (e.g. radioembolisation with chemotherapy - SIRFLOX) or hybrid therapies such as gene therapy delivery. The belief of many medical experts is that with so many specialities evolving and such a wealth of knowledge available, doctors must pool their expertise if medicine is to advance into a new age, both in terms of research, and in terms of provision of care.

One team, one goal
This trend can be clearly seen in the growing number of multidisciplinary clinical set-ups. This philosophy can be fully embraced as an ad hoc clinic (see page 24 for information on the Johns Hopkins' Multidisciplinary Liver Tumor Clinic), or it can be as simple as better collaboration agreements within existing hospital structures. It is widely recognised that a multidisciplinary evaluation of patient cases can improve treatment outcomes - rather than being shunted from specialist to specialist, the patient is sent to the right one from the beginning.

> Doctors must pool their expertise if medicine is to advance into a new age

These factors are essential if IR is to offer its advantages and opportunities to eligible patients. The traditional IR who hid in his lab devising his new treatments is no longer sustainable, and indeed, is no longer a reality. IRs have realised that the onus is on them to approach their clinical colleagues, to produce scientific data and to see their patients. Although obstacles still exist, many are making good headway in this area, and have gained the respect and trust of both their colleagues and their patients, establishing themselves as full clinical members of the hospital team. This impressive trend must be continued and embraced if IR is to reach its full potential.

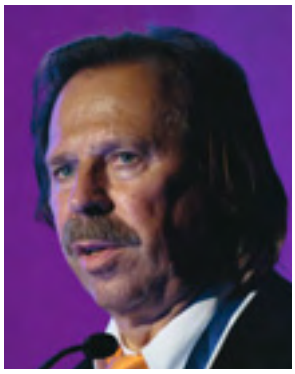
Good for patient? Good for hospital!
Like any treatment, IR treatments must be matched to the patients they are suitable for, and carried out by trained professionals. When they are, they can provide many benefits for both patient and hospital. The patient can benefit by undergoing less invasive procedures that allow for fewer potential complications and a shorter hospital stay; they may experience less nausea and scarring; they may be offered relief from their complications, such as superior vena cava syndrome; those with progressed tumours may even be become eligible for life-saving surgical resection or transplant, or have their treatment made more effective through IR support. These are all advantages for the hospital too: in requiring shorter hospital stays, overcrowding and costs can be reduced; by offering sought-after treatments, demand may increase; and by encouraging a multidisciplinary approach, treatment becomes more efficient. It is in everyone's interest to ensure that all patients are offered the full range of potential treatments, and based on early clinical data, IR must be included in this category.

> Less invasive procedures ... allow for fewer potential complications and a shorter hospital stay

www.cancer.gov
www.macmillan.org.uk
www.cirse.org
www.cc.nih.gov/centerio
radiology.usc.edu/io

A New Era of Teamwork

Dr. Vincenzo Mazzaferro



Prof. Hans-Joachim Schmoll

While originally reserved for no-hope patients, interventional methods are being increasingly employed in the early stages of cancer treatment. Accordingly, recent data has shown excellent results for many modalities, and patients are highly enthusiastic about their experiences.

This positive data has led many oncologists to consider IR at earlier stages of the treatment process, particularly as an adjuvant treatment.

- Improved screening means that cancers are being detected earlier (and smaller), and for small, isolated tumours, ablative techniques may be a preferable control measure to surgical resection.
- An organ riddled with tumours is impossible to deal with via surgical resection. Local delivery of chemotherapy or radio-agents can help treat multiple lesions, while leaving the organ itself more or less intact.
- Other patients require an organ transplant, but may find that their tumour size excludes them. IR may help shrink the tumour and allow surgeons to perform their life-saving transplants.

These are merely examples of the role IR can play within a well-structured oncology team.

Vincenzo Mazzaferro, renowned surgeon and author of the Milan Criteria for liver transplantation, spoke at the European Conference on Interventional Radiology (ECIO). He is an ILCA (International Liver Cancer Association) Council member, a group that lent their support to ECIO. In his lectures, he put forward evidence to suggest that IR procedures can improve patients' eligibility for surgical treatment: "Data comparing conventional and modern approaches to liver metastases show that surgery, often in combination with chemotherapy or portal vein embolisation (PVE), can now be used to treat more patients – PVE increases the pool of patients who can safely undergo potentially curative hepatic resection."

Colorectal cancer specialist and ESMO (European Society of Medical Oncology) board member, Hans-Joachim Schmoll, agrees, and points out the necessity for doctors to correctly identify the most appropriate treatment approach:
"Different cancers have different properties, and it's this that decides the treatment needed. Pancreatic cancers tend to metastasise to different areas, and applying local interventional techniques to these multiple metastases is an ineffective way of dealing with the underlying disease. However, many colorectal cancer patients have their metastatic disease limited to one or two organs, so applying a local treatment to affected organs is an effective way of tackling the disease, which is where IR can play a major role."

Both men highlight the importance of collaboration between specialities. Prof. Schmoll believes that "the most important concept in oncology today is that of the multidisciplinary team." Dr. Mazzaferro also advocates a multidisciplinary approach to cancer treatment, as individual specialists reach "a kind of plateau with his/her procedure." When all doctors lend their expertise to a case, the patient benefits from having all options available to them.

IR techniques to fight cancer are a valuable addition to the cache of weapons available to doctors. There is no golden bullet for cancer, and it is important that all options are properly considered to ensure optimal patient care.

Delivering Hope

Yttrium-90 Radioembolisation of Liver Tumours

Although real-life heroes might seem rare, patients for whom there seems to be no hope are saved every day by medical innovation. When a procedure is in its infancy and the indications and outcomes are unsure, a unique combination of intelligent foresight, talented doctors and courageous patients are needed to propel the procedure from the theoretical realm to the clinical.

Patient - José Luis Giménez

José Luis Giménez is a 53-year-old primary school teacher. In January 2003, he was in for a shock - he was diagnosed with hepatocellular carcinoma (HCC). Based on tumour staging, Mr. Giménez was considered a candidate for liver transplantation. In order to prevent the disease from progressing while he waited for a transplant, two transarterial embolisation treatments were administered at the Clínica Universidad de Navarra, the first in March 2003 and the second in April of the same year, neither of which achieved their objective.

On confirming that the treatment had been unsuccessful and that the disease had advanced, Mr. Giménez was taken off the waiting list for a liver transplant. The situation was not looking promising. In September 2003, the doctors offered Mr. Giménez an experimental treatment - radioembolisation with Yttrium-90-labelled microspheres. He courageously decided to try it, and became the first person in Spain to be treated by this technique.

“I was convinced that it was all going to work out well because I had a lot of trust in Drs. Quiroga and Sangro, and their team. They told me that it was a procedure that was producing good results and that in principal, it didn’t have any downsides. Indeed, I had noted some improvement with the embolisations and since everything was going well, I decided to go ahead. I didn’t doubt it for a second”.

The patient's recovery

After the treatment, Mr. Giménez progressed favourably and the liver lesions decreased slightly in size and remained inactive from a radiological point of view (i.e. they no longer showed contrast enhancement). Thus, in April 2006, he was readmitted to the liver transplant list. Finally, in September 2006, transplantation was performed successfully and Mr. Giménez is currently free from hepatocellular carcinoma and leading a normal life.

Through the use of radioembolisation, a patient who had lost the opportunity to receive a curative treatment, a liver transplantation, again became eligible for this treatment, even after two previous bland embolisations had failed.

L-R, Dr. José Ignacio Herrero (Hepatology Department), Dr. Bruno Sangro, José Luis Giménez (patient)

“As a result of the treatment, I felt much better. Up to the point that I didn’t understand why they then told me about the possibility of having a transplant as I felt fine. But it’s true that before this treatment, the transplant was unfeasible and now, I have had one."

Hepatologist - Dr. Bruno Sangro

“In the last 2-3 decades, we have observed how interventional techniques may provide excellent results in terms of tumour destruction and improvement of quality of life, and even overall survival in some cases, with few adverse events. And this is true for all centres experienced in using both surgical and interventional radiology techniques.”

> "Before this treatment, the transplant was unfeasible and now, I have had one"

José Ignacio Bilbao, Interventional Radiologist

IR - Prof. José Ignacio Bilbao

"An embolus is something that moves from one location to another; that migrates within a vessel. In radioembolisation, we use embolic particles to transport and deliver radiation within the tumour. We do not want to produce ischaemia or occlude the vessel, as a major enemy of radiation is ischaemia. Without oxygen, the radiation is not active against the DNA nuclei. We deliver the radiation by means of very small particles that go deep within the tumour. These particles have a radioisotope, Yttrium-90, safely bound to them, and once the particles are in place, they deliver radiation. Even in a very thin person, the radiation will never go through the skin, so it is a very safe procedure and can be performed on an outpatient basis, although our patients usually remain overnight."

Advantages

"An advantage of radioembolisation is that it can be used in patients with cirrhosis or portal thrombosis. Any patient that is to have a hepatic procedure needs to have a good liver function, so we send patients for laboratory tests to evaluate the liver function - the bilirubin level is very demonstrative of probable outcomes. In some institutions, they work with a threshold of 2.5; we work with 2.1. Studies by the European Network of Radioembolisation in HCC have shown that up to 75% of patients have cirrhosis, and up to 60% have some kind of portal thrombosis. You can have HCC in non-cirrhotic patients, but this true mainly in Asian countries. In Europe, HCC is primarily an evolution of cirrhosis."

Team effort

"Radioembolisation is a completely multidisciplinary procedure. It is essential to have the input of good oncologists, hepatologists, nuclear medicine physicians, diagnostic and interventional radiologists. On top of these experts, you need to have good techniques and excellent facilities. It needs to take place where there is a well-trained team - so mainly university centres, but not exclusively. There are currently many centres in Germany and Italy, and a few in Spain, the UK, Belgium, Austria, France, Greece, Turkey and Portugal. This multidisciplinary cooperation is not only necessary for the procedure itself - if patients are to receive suitable treatments, as Mr. Giménez did, physicians must be aware of all available treatments, and the indications and contra-indications for each."

The first Spanish centre

The Clínica Universidad de Navarra is the main Spanish hospital where radioembolisation with Yttrium-90-labelled spheres is carried out. At present, the Clínica Universidad de Navarra is also one of the busiest centres in Europe in terms of the application of this therapeutic procedure. In fact, in the last seven years, more than 300 treatments of this type have been carried out - an average of 40-50 radioembolisations per year.

Clínica Universidad de Navarra

Indications

Radioembolisation with Yttrium-90-labelled spheres is a treatment indicated for primary hepatic tumours (basically, HCCs). While other endovascular treatments (such as chemoembolisation) are not recommended for HCCs with portal vein thrombosis, radioembolisation does not have these restrictions, because it does not occlude the arterial vessels.

This procedure is also indicated for secondary liver tumours of metastatic origin. Although colorectal cancer metastases are among those most commonly found at the Clínica Universidad de Navarra, the procedure has also been applied in secondary breast, renal, lung and neuroendocrine tumours.

From the experience accumulated in the Clínica Universidad de Navarra, the most important factor is that the tumours are hypervascular, regardless of their origin. Since there has been considerable worldwide experience with cases of metastatic colorectal tumours, some studies have shown that its combination with chemotherapy treatments improves the results of the chemotherapy. Indeed, studies which define the best time to give combined treatment are ongoing. In terms of primary hepatic tumours, tumour growth can be controlled in more than 90% of cases for long periods and there are data suggesting that it improves the survival in most of the patients treated.

Images reproduced by kind permission of Clínica Universidad de Navarra

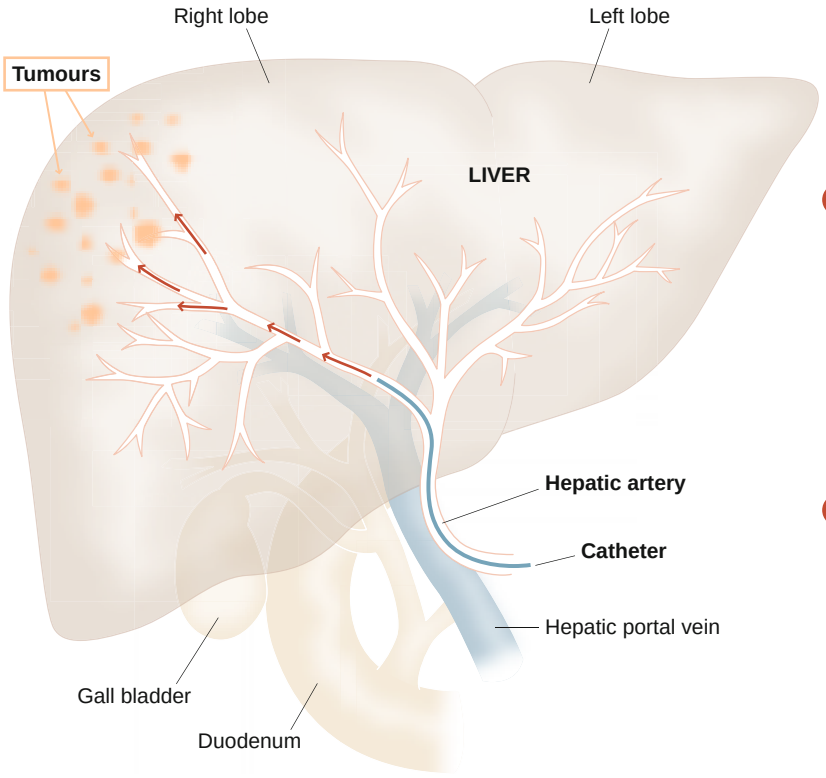
>

The procedure

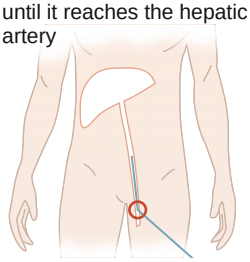
Aside from the clinical advantages that radioembolisation offers, another major advantage is that the results can be quite easily compared. With other intra-arterial procedures such as chemoembolisation, there can be multiple ways of performing it, making it very difficult to establish its efficacy rate in retrospective studies. With radioembolisation, however, the dose is always very precisely calculated, and outcomes can be more easily classified. In a world that relies on empirical data to justify medical treatments, this is a big advantage for all who want to evaluate its efficacy, and allows for easier exchange of information among clinicians. Indeed, several trials are currently underway that incorporate radioembolisation into a first-line treatment schedule (see page 35).

Radioembolisation

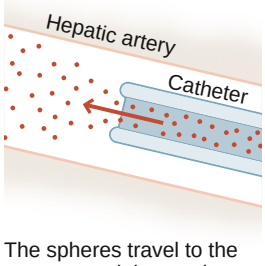
This technique is particularly recommended to treat multiple tumours. Tiny radioactive spheres are injected directly into the artery that supplies the tumour with blood. These microspheres are delivered to the affected regions and they damage the tumour cells by emitting radiation.



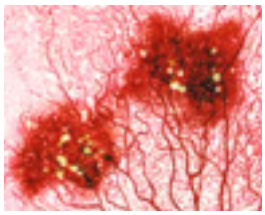
1 A catheter is inserted through the femoral artery until it reaches the hepatic artery



2 The microspheres loaded with Yttrium-90 are released into the hepatic artery

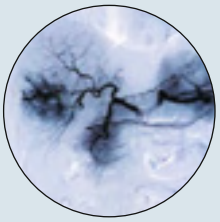


3 The spheres travel to the tumours and they emit radiation that destroys them



Pre-procedural investigations

These are carried out a week before the treatment commences and their aim is to ensure that the radioactive spheres don't attack healthy tissues and produce damage in the patient.



Hepatic arteriography

The arterial anatomy of the liver is studied in detail to identify the vessels that irrigate the tumour.

Simulation of the treatment

Instead of radioactive spheres, albumin macroaggregates are injected that are labelled with technetium to study where they settle.

Calculation of the dose

The treatment is specifically designed for each individual depending on the characteristics of the tumour and of the patient.

With thanks to Prof. José Ignacio Bilbao, Dr. Bruno Sangro and Mr. Javier Urrutia for their kind contribution

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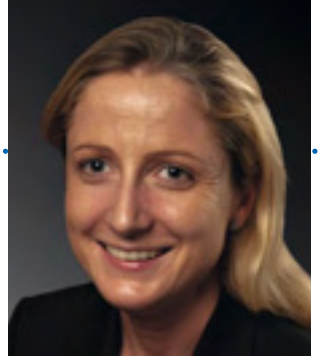
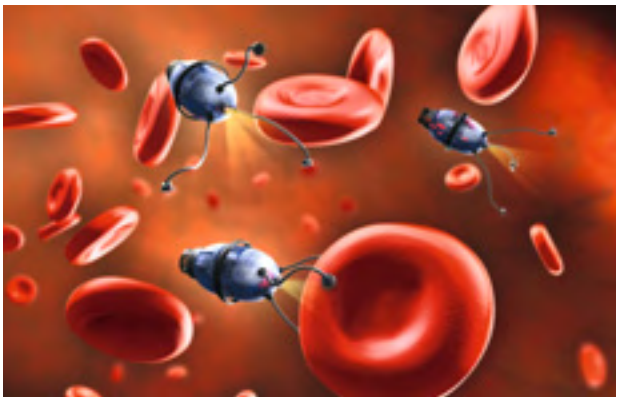
The Huge Impact of Tiny Particles





© Andrea Danti

Technology everywhere is getting smaller – micro this and nano that – and medical technology is no exception. Doctors are now working on the truly nano level, with active particles that measure only one billionth of a metre in width.

Dr. Aoife Keeling, IR at Beaumont Hospital in Dublin, explains the potential impacts of nanomedicine.

"The small particles used in nanotechnology have different properties than that of larger particles, and it's these properties that are of interest to scientists. The main role for both medicine generally and for radiology specifically is that of two areas: one is imaging, and the other is therapy."

How can nanoparticles help improve imaging, and how does this help IR?

"Imaging is vital to the practice of IR: it's image-guided interventions. Certain nanoparticles, such as iron oxide particles, can be used as contrast agents for MRI to enhance the image. So far, it has mainly been used for imaging lymph nodes in patients with a known cancer: to see if that cancer has spread outside the body part that it was initially in, and affected the lymph nodes. IRs can inject nanoparticles directly into tumours under image-guidance, and then image with MRI to see where those particles travel. This is called sentinel lymph node mapping, and has been around for many years, but now one can use nanoparticles to do it, which can reduce patient exposure to radio-isotopes and ionising radiation. The lymph nodes can then be biopsied using MRI-guidance to determine if they are involved with the tumour."

What are its therapeutic applications?

"Nanotechnology has great therapeutic potential. Currently, for most cancers, the first-line therapy is surgery, often in combination with chemotherapy. However, the limitation of chemotherapy is the systemic delivery of these medicines. While many work extremely well, the systemic side-effects limit the dose that you're able to give the patients. Nanoparticles can act as carriers that can be attached to the chemotherapy agent, allowing site-specific delivery, ensuring that a concentrated chemotherapy dosage is delivered within the tumour itself where it is needed, rather than to the whole body, eliminating the systemic side-effects."

Does IR have any role in these treatments?

"There are a number of carriers out there now that have different properties based on their structure, their size, how they attach to antibodies, thus one can choose specific agents for the pathway that you wish to target. IR's involvement is in the delivery of these agents. Local delivery can be achieved by means of direct injection into the tumour with an image-guided needle (similar to a biopsy) or injection into the tumour via the artery (like the TACE procedure). Both methods allow for a concentration of the agent in the tumour, and a reduction in systemic side-effects. Because they're attached to the nanoparticles, the chemotherapy agent can also be released in a controlled manner."

It's a very futuristic field – how far have we come in its development?

"At this stage, nanomedicine is still somewhat experimental. There are plenty of studies being done, mostly in animal models, and these are showing great promise. One area of research is synergy – augmenting the effect of some other established treatment. Different groups have shown benefit from combining chemotherapy-loaded nanoparticles with both radiofrequency ablation and external beam radiation – it seems to intensify the results. An Italian group is looking at intra-arterial delivery of chemotherapy-loaded nanoparticles, and they've shown a reduction of tumour cells."

What does the future hold for nanomedicine?

"This is all still in its infancy, but all results so far have been positive. What we need to look at next is can these nanoparticles or nanocarriers make current chemotherapies more effective, and could older, less effective chemotherapy agents be improved by adding nanoparticles – could their properties be changed? This has been demonstrated already with mitoxantrone, a chemotherapy agent – early data shows a survival advantage of 2.2 months in HCC patients, which is very exciting."

Do you think we will ever be able to develop nanorobots for medical use?

"Nanorobots certainly aren't as far-fetched as they might sound. At the moment, nano-channel delivery systems are being developed, which are small devices that are percutaneously implanted adjacent to the tumour, and these are loaded with nanoparticles. They then control the release of whatever is coated onto the nanoparticles, be it a chemotherapy agent, an anti-inflammatory agent, or an agent to reduce atherosclerosis.
Nanomedicine raises huge opportunities for the medical world, and it's important that IR is there to help deliver it."

Dr. Thierry de Baère
Villejuif, France

"It is important to have the support of the head of your hospital - mine has a strong interest in imaging and really supports us. He encourages visitors to the hospital to come to our interventional department and they are always impressed with our clear 3D images and seeing the RF probe expanded in the tumour. He realises the need to invest money in image-guided therapy, because it is a valuable resource for a hospital."

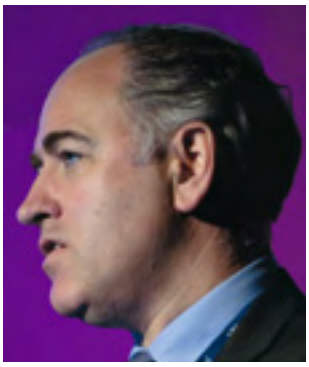
Prof. Thomas Vogl
Frankfurt am Main, Germany

"The medicine of the future will be data-based, and patients will access this information via the internet more often. Patients love the idea of having very precise therapy with a low rate of side-effects, done in a quick fashion and improving their quality of life. Hospital administration will continue to support these procedures, because they will also see that it attracts patients to the hospital."

Communication and Collaboration

Prof. Philippe Pereira
Heilbronn, Germany

"Intervention oncology is, from a financial point of view, quite interesting for a hospital. Although some interventions may initially cost as much as a surgical operation, the difference is that after chemoembolisation or radiofrequency ablation, the patient leaves the hospital after 1 or 2 days rather than spending 5 days in ICU, and that is very cost-effective."



Dr. David Breen
Southampton, UK

"Cancers are getting smaller because radiology is detecting and characterising them at an earlier stage. You don't need big surgery for cancers that are being appreciated at an increasingly smaller size. Not only are surgical procedures a major undertaking for the patient, but they're highly costly as well, and administrators and patients alike are starting to realise this."

Dr. Jim Caridi
Gainesville, FL, USA

"I would advise any hospital administrator to embrace these new technologies because the strong data and good patient feedback show that these treatments are going to be in great demand, so you might as well be on the forefront as opposed to trying to catch up later. If you are seen as a hospital that will do everything to help your patients, that will always stand to you."

Dr. Raj Narayanan
Miami, FL, USA

"IR is no longer just about doing the procedure and forgetting the patient. You need to build up a thorough understanding of oncology. You need to build credibility by actively participating in a multidisciplinary group and routinely showing your follow-up results to them. Your honesty and involvement builds their confidence and they feel their patients are taken care of. Specialists in our multidisciplinary group definitely welcome the fact that we are seeing their patients in clinic and follow-up, and that we're more serious about taking clinical responsibility for these patients."

Why IR is making waves among hospital managers

Prof. Szczerbo-Trojanowska
Lublin, Poland

"Nowadays, medicine is no longer a one-man show and there is no longer one speciality which is the driving force. All the new interventions and new ideas are usually born on the crossroads of many specialities. Further progress in our speciality is impossible without the involvement of molecular biology, physics, genetics and clinical disciplines including oncology. Broad cooperation is absolutely crucial, as each of us is just giving a part to the exciting new developments."

Dr. Tobias Jakobs
Munich, Germany

"Only a few centres have their own beds, so we IRs rely on referrals and need the support of gastroenterologists, hepatologists, oncologists and surgeons. You have to win this support by presenting good results. Literature is important, but this is an initial step to get the first referral. They have to see the positive outcomes with their own eyes. We need to confirm what's published, and then they will start referring. That's what worked for me."

Worldview

The difference between working in a Cancer Centre and a General Hospital
Bordeaux/France

"The main differences are being able to focus on one disease and having more exchanges with other specialists during multidisciplinary meetings. It is also easier for us to have true clinical involvement in consultations and follow-ups. In France, another advantage could be the ideal size of dedicated cancer centres - neither too big nor too small, and all are open to innovations."
Dr. Jean Palussiere, Institute Bergonié

The Institute Bergonié is renowned for diagnosing rare forms of cancer. The IR unit of the institute was created in 1999 and carries out around 650 procedures each year.
www.bergonie.org

A possible new frontier for IO
Maryland/USA

The Sidney Kimmel Comprehensive Cancer Centre of Johns Hopkins forms a crucial part of the leading health institution Johns Hopkins. Twenty years after its establishment, experts in the centre continue to provide patients with excellent care while at the same time being active in research and prevention programmes. A new form of treatment is slowly being added to those offered at the institute - robotics - one of the areas which could also be a new frontier for IO.
www.hopkinsmedicine.org/kimmel_cancer_center

Why Interventional Oncology was introduced into my centre
Buenos Aires/Argentina

"The application of minimally invasive techniques at this centre began in 1992 in order to improve the quality of the treatments offered to patients. The techniques were introduced by a group of doctors who were trained at different centres in Europe and the USA."
Prof. Mariano Gimenez, Buenos Aires University Hospital

The Hospital of the University of Buenos Aires sees around 2,300 patients from throughout the country per year and is home to one of largest cancer centres in Argentina for abdominal cancer.
www.hospitaldeclinicas.uba.ar

Why multidisciplinary cooperation is so important
Cairo/Egypt

The Egyptian National Cancer Institute is one of the largest institutions for cancer care in the Middle East. With the wealth of knowledge that the institute's numerous cancer specialists bring, interdisciplinary cooperation ensures that patients get the best treatment possible. The institute is committed to its "multidisciplinary approach in cancer management" in which different specialties "cooperate rather than compete" - an approach that is known to bring the most benefits to patients.
www.nci.edu.eg

Why patients are referred to my IR unit
Nagoya/Japan

"Physicians and surgeons in our centre and from other hospitals refer patients who require IR treatment to our unit because they understand that IR is minimally invasive and is also quick and highly effective."
Dr. Yoshitaka Inaba, Aichi Cancer Centre

As one of the leading medical institutions in Japan, the Aichi Cancer Centre is well known for excellence in the treatment of liver metastases. The Diagnostic and Interventional Radiology Department also boasts numerous cutting-edge imaging tools.
www.pref.aichi.jp/cancer-center/english

National Cancer Centre Singapore
SingHealth

What makes a cancer centre "comprehensive"?
Singapore City/Singapore

The National Cancer Centre of Singapore (NCCS) is a national and regional centre of excellence in the areas of research, education and clinical practice. Physicians from various medical specialties, including IRs, work closely together to ensure patients receive appropriate and effective treatment. These and other characteristics are what give the NCCS its "comprehensive" character. The NCCS has also led or been involved in numerous cutting-edge research projects in the areas of kidney and stomach cancer.
www.nccs.com.sg

How IRs are helping in my institute
Milan/Italy

"The European Institute of Oncology is one of the most important centres for breast cancer worldwide. The need for IRs' help is mainly evident in the management of metastatic patients. We recently started a pilot study for treating small breast cancers by means of High Intensity Focused Ultrasound in order to avoid lumpectomy. I believe this will be the future - "non-invasive" treatments for that form of cancer."
Dr. Franco Orsi, the European Institute of Oncology

The European Institute of Oncology is a world-famous, non-profit institution that prides itself on its innovative models for cancer care and research.
www.ieo.it

How the patient's treatment plan is decided in my centre
Mumbai/India

"At Tata Medical Centre, the treatment of patient is decided by a multidisciplinary team of medical, surgical, and radiation oncologists along with pathologists and diagnostic and interventional radiologists. There are Disease Management Groups (DMG) for each type of malignancy and the management is decided in the Joint Clinic, which is a multidisciplinary team. The interventional radiologist is an integral part of the DMGs."
Dr. Suyash S. Kulkarni, Tata Memorial Centre

Tata Memorial Centre places great emphasis on its mandate to provide excellent "medical service, education and research," areas in which the centre's IRs are actively involved.
www.tmckolkata.com

5 minutes with...

Prof. Jean-François Geschwind

Johns Hopkins University School of Medicine has many enviable assets, amongst which can be counted renowned researcher, Prof. Jean-François Geschwind, and his pet project, the Multidisciplinary Liver Tumor Clinic (or Multi-D): a disease-oriented initiative which aims to provide liver cancer patients with the most comprehensive and efficient care possible. IQ talks to him about the Multi-D, best collaboration methods and their economic benefits.

The Multi-D is a very dynamic clinical structure - how was it established?

This is first and foremost for the patient's benefit. We have had a multidisciplinary liver cancer tumour board for years now, so it was logical to develop a true multidisciplinary clinic. But to finally create this multi-D clinic and resolve the last few administrative problems, we needed someone to step up, and here, I have to give credit to my surgical oncology colleague who was able to achieve it. It was vital to have a business plan, even if it is not so sophisticated. After presenting ours to hospital management, they were on board. We raised local awareness through lectures and CME activities through dinners that were held in the region, promoting our vision of complete assessment of patients. It took us 10 years of tumour board experience to finally establish a multidisciplinary clinic, and now the patient, depending on the diagnosis, can be seen by different people all in one visit - hepatology, surgery, interventional radiology, or transplant.

Are there many centres in the US (or worldwide) who offer similar services to what the Multi-D provides?

I think this notion is gaining acceptance, but there is a lot of room to grow. There are many examples of other clinical subspecialties getting together to promote their programmes and expertise, but a programme like ours that encompasses all specialties involved in the care of patients with liver cancer is still pretty rare.

How can other IRs get involved in multidisciplinary clinics? What advice would you give?

The first thing you need is clinical credibility, so you need to be able to demonstrate to your clinical colleagues that you can manage patients, that you're doing a good job, and that, more importantly, you have an infrastructure to achieve these goals. Infrastructure requires nurse schedulers who can screen phone calls from referring physicians and answer simple questions from patients; physician extenders (which is something that maybe isn't common in Europe); and nurse practitioners who can manage the patients during procedures. This shows your clinical colleagues that you're committed to taking care of your patients.

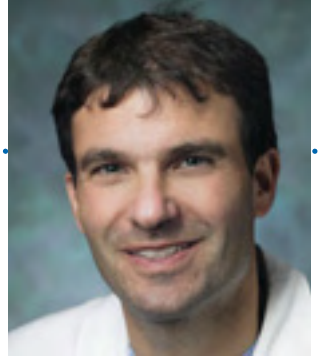
Once this clinical infrastructure is in place, two additional things are really crucial – firstly, the organisation of a weekly forum (tumour board) in which appropriate discussion of patient management and best therapeutic options are discussed in detail (and you can organise this even without having a clinical infrastructure); and then the establishment of a meaningful cooperation or collaboration with your clinical colleagues so you can participate in (and eventually lead) clinical trials.

So an IR needs to organise certain resources to show that he's serious about longitudinal care – how can an IR go about securing these things?

It's not easy at all – it's best to have some financial evidence of IR's importance in generating precious income for the hospital, such as discharges (if IRs have admitting privileges), clinic visits and downstream revenues to radiology, especially through the "capture" of patients. Once the hospital sees the financial ramifications of a successful IR practice, it is easier to convince them. In addition, IR practice is critical to any hospital. Without IR, there would be no possibility for a hospital to have sophisticated, and of course, money-generating programmes such as transplantation or cardiothoracic surgery. It is much more efficient and less costly for IR to do these procedures.

We hear a lot about turf wars between different disciplines – how did you achieve such a good relationship with the other specialities?

When people say all politics is local, it's really applicable in this case. If you have a mutually-respectful relationship with your colleagues, based on clinical ability, they will respect you. You take care of their patients and they do yours; you also send them patients, so it's a two-way street. And in the US especially, everyone benefits from such an arrangement because at the end of the day, it's about distribution of money. When people think there's a win-win strategy, they will do whatever it takes to make it work – and you're more powerful as a group than if you're isolated. It is through these constant and fruitful interactions with clinical colleagues that you gain their trust.



Prof. Jean-François (Jeff) Geschwind joined the faculty of the prestigious Johns Hopkins University School of Medicine in 1998 as an assistant professor, was appointed Division Director of Cardiovascular and Interventional Radiology in 2002, and Director of the Interventional Radiology Center in 2008. In 2007, he was promoted to Professor of Radiology, Surgery and Oncology.

Prof. Geschwind has authored or co-authored more than 250 published scientific articles and abstracts on interventional oncology, and co-authored "Interventional Oncology Principles and Practice" - the first book dedicated to interventional oncology. He holds multiple awards, is on the editorial board of four medical journals, and is an active member of numerous American and international oncology and interventional societies.

There's a huge difference between the USA and Europe in terms of administrative structures, but is there anything that European doctors can learn from the way things are done in America?

It's hard to know, because I left Europe 25 years ago, but from what I hear, if you remove the financial incentive, there may be actually more of a reason for people to collaborate. Most European physicians are salaried, and it doesn't really matter if they treat more patients than the next guy, so there may actually be a stronger reason for them to assemble. In the US, there's always the money issue, even in academic institutions. Despite these potential difficulties related to money, there is always the genuine desire in the US to make things work; the so-called "win-win" strategy. If there are obstacles, and there always are, you navigate past them and eventually you find a solution.

There are obvious clinical benefits to a multidisciplinary approach involving IR, but what about the economic benefits?

If you look at the future of medicine, which is so specialised, you really need a multidisciplinary approach to provide comprehensive patient care. It has become very difficult for any one physician to know everything about a certain disease and the various therapeutic options. If you are part of that multidisciplinary group, then you hear what your colleagues are doing, and you can guarantee optimum management for patients. As a result, there is no redundancy in care, and costs can be minimised because you have a group of experts that decide on therapy in unison. It's streamlined – instead of having a patient scheduled to see physician x, y or z, wasting time in terms of initiation of therapy, you've got all that in one setting.

Where do you see IR in 10 year's time? Do you think it will have a bigger "market share" of patients?

The future for image-guided interventions in cancer is extremely bright and I would not be surprised if it were to grow tremendously in the next decade. But which specialty is going to be doing it is a harder thing to predict. If we want to avoid what happened with peripheral vascular disease, we as interventional radiologists have to remain ahead of the curve and become the true leaders in research. We have to be creative and show we can do fundamental research in addition to running clinical trials. We also must have a presence at meetings organised by the other specialties. We are the voice of interventional radiology, and if we do not attend these meetings, we will be forgotten. We have a collective responsibility to have a presence at these meetings, to publish in their journals and show we exist and demonstrate that what we do is beneficial to patients.

In what areas will IR be most involved?

With the developments in imaging and image-guidance tools, and as cancer therapies are becoming more individualised, the role of loco-regional treatments will increase even more. Both catheter-based intra-arterial therapies such as drug-eluting microspheres and Y-90, and percutaneous ablative techniques will continue to do very well. Regarding intra-arterial therapies, we need to get access to better drugs, i.e. some that are more effective and less toxic because they target specific pathways in cancer cells; we also need better drug-delivery systems that will allow more effective drug delivery to the tumour; and maximise the treatments we already have by combining them with systemically-delivered targeted drugs. In this way, we will be able to go beyond liver cancer and treat many other cancers. I also think HIFU will play a growing role either as a direct ablation method or as a way to increase local drug delivery to tumours. If I had to predict which cancers we will affect most, I would still think it would be liver (primary and metastatic), lung and kidney. Those are still the top 3, but our involvement in other cancers such as breast and prostate for example will also continue to increase.

You are a member of a medical field that generally struggles to get recognition from non-interventional colleagues, and yet have been the recipient of many awards and much praise – what has been the secret of your success?

Thanks for the compliment. Research was key for me. I knew that research generated credibility and I guess I was right. I had examples from my father (a retired cardiologist) and uncle (a retired neurologist), and mentors throughout my career that lead me on this path. The other aspect is clinical reputation. A lot of credit should go to those who created the first IR division at Johns Hopkins 25 years ago, as they had the foresight to recognise the importance of a robust clinical practice.

Overcoming the Odds

TACE - Transarterial Chemoembolisation

The Patient

Fred Haselbauer is an ordinary man. And like one in three ordinary men, he discovered that he had cancer. A resident of Ormond Beach, Florida, Fred had worked for almost 50 years with cranes and bulldozers. He and his wife, Kathy, raised a daughter together, who will be finishing college in summer 2011. Upon his retirement, he took up a volunteer position at a local hospital. But the shock discovery that he had six malignant tumours on his liver changed all that.

"About four years ago, I was sick, and the tests performed revealed a mass, about the size of a quarter, on my liver. A biopsy showed it to be benign, so I opted to do nothing about it. Four years later, during a routine check-up, they found six of them, but I wasn't feeling bad, or sick, or anything. But when they did the biopsy on the others, it came back positive. So I now had six tumours on my liver. And at that point, my doctor said, 'Fred, you have a problem: if you don't take care of this now, you're going to die.'

"Then he said, 'I'm going to see if I can get you hooked up with the Shands Cancer Hospital, they're doing some research work over there, and I think you might just fit into this.' So he set me up with an appointment at the Shands Hospital, where they told me what was involved, and asked if I was interested. I was very open-minded and prepared to consider anything. I'm aware that there are quite a few different programmes going on, and based on the doctors' recommendations, I felt I had no other choice, so I agreed to it.

"They set up an appointment for me for a week later and I met Dr. Caridi, who did the TACE procedure. He said, 'you have six, but I can't treat 'em all now," so he went to one side and, amazingly enough, was able to get four of them. So then I waited a month or two, and he did another TACE procedure to get the other two. He told me that the CT scans for the original four were looking good, and he said, 'they're all dead, and the procedure I did today to remove the other two went very, very well.' So they got all six!

"Dr. Caridi was excellent, he did a great job. And now, from what I understand, all of the tumours are destroyed, and I just have to continue with the medication until the end of November, when another final scan will hopefully confirm that there's no recurrence.

"I wouldn't wish this on anyone, but many people unfortunately do get cancers. Should it happen, I would advise any friend of mine to go through this procedure. This is definitely the way to go, because it takes one day to go to the hospital, you spend a night and then you go home. How much simpler could that be? You have to continuously give blood work, but that's quickly arranged and from that, they monitor other parts of your health. I've had other problems that they've given me medication for - they're nice people, and I really like the way they handled me. I would recommend this to anyone who has this problem and needs a procedure done."

Fred on a recent holiday in Austria

Fred enjoying the Austrian delicacies with his daughter

Shands Hospital, Florida, USA

Dr. Caridi, Fred's IR, who performed his life-changing TACE procedure

One of the Angiorooms at the Shands Hospital, University of Florida

The IR

Dr. Jim Caridi is an interventional radiologist at Shands Hospital at the University of Florida. He performs a wide range of IR procedures, from trauma cases to cancers. He and his colleagues treated Mr. Haselbauer's liver tumours using interventional techniques.

"Early in 2010, a 71-year-old gentleman with a history of hepatitis C presented at our hospital with multifocal HCC. A CT-scan showed multiple bilobed large enhancing lesions. His case was discussed at our multidisciplinary hepatobiliary conference. As his liver tumours were outside the Milan criteria* for transplant, and were too numerous for resection, drug-eluting beads loaded with the cancer-fighting drug, doxorubicin, (DEBDOX) were recommended. These were delivered using transarterial chemoembolisation (TACE).

"DEBDOX (drug eluting beads with doxorubicin) was recommended due to the extensive tumour burden. The advantage of using DEBDOX over the alternatives was that it does not affect the underlying function of the liver like some other therapies. Normally, patients with hepatocellular have compromised liver disease and certain treatments can make this worse. As another benefit Debdox has less systemic chemotherapy side-effects than its alternatives.

"As he had tumours on both liver lobes, he was scheduled for a two-phase procedure, treating one lobe per session. The first session treated the 4 lesions on the right lobe. As with any medical procedure, there is always a risk of complications. In this case, one of the lesions experienced a phenomenon that sometimes occurs with tumours.

"The vessels are fragile and when embolised, may spontaneously bleed. This was treated on the spot with no consequences.

"A one-month follow-up CT demonstrated no residual enhancement in the treated lesions. The angiogram obtained for treatment of the left lobe concurred with the CT. The left lobe was subsequently treated as planned.

"We're delighted that Mr. Haselbauer's tumours have responded to treatment, and wish him all the best in his recovery."

** generally accepted criteria for liver cancer evaluation*

Transarterial Chemoembolisation
The TACE concept has been around for many years now. Drug-soaked particles are injected through a catheter that has been fed directly to the tumour under image-guidance. This has a two-pronged attack: it causes tumour ischaemia (so it blocks the blood flow to the tumour) and at the same time gives a higher dose of chemotherapy, over long period of time.
The way they used to deliver chemotherapy before, the drug dissipated quickly and went into the blood stream and the patient would have unpleasant side-effects. When these drugs are attached to a particle, it is eluted slowly, and it doesn't get into a higher level in the blood. The materials we have used to deliver the drugs have improved over the years, and using Doxyrubin-loaded beads obtain great results, releasing the drugs very steadily and reducing side-effects even further.

Irreversible Electroporation
A "Hole" New Approach to Cancer Care

It is safe to say that few things have changed the way we live more than electricity. Just imagine how life would be without our computers, telephones and televisions! Centuries after its boom in the industrial revolution, electricity continues to play a vital role in modern life.

From electric cars to electric blankets, there is no shortage of ways in which we choose to employ the wonder that is electricity. More recently, medical researchers have brought us a new take on the "electrical hole punch" - not the kind you find on your office desk, but one that harbours immense potential for minimally invasive cancer care. This breakthrough procedure, known as Irreversible Electroporation, is based on a medical phenomenon that occurs when high electrical pulses are passed through cells, creating large holes in their cell membranes.

What is electroporation?

- Electroporation occurs when electric pulses are applied to cells, causing holes in the lipid bi-layer of their cell membranes
- Electroporation can be reversible - causing only temporary damage to the membrane
- Reversible electroporation is used to enhance the effect of chemotherapeutic drugs in a technique known as Electrochemotherapy

What is Irreversible Electroporation (IRE)?

- Electroporation becomes "irreversible" when longer and stronger electrical pulses are used to create permanent holes in the cell membrane that cause cell death
- Irreversible electroporation is used in the food industry for sterilising and pre-processing food products and is known to be an effective means of destroying bacteria and amoebae in contaminated water

Why is Irreversible Electroporation different?

Electroporation is not a new discovery, as it was observed as far back as 1754 by the French scientist Jean Antoine Nollet during one of his experiments on electricity. What is new is the use of IRE in the treatment of cancerous lesions, which was developed by Dr. Boris Rubinsky of the University of California in Berkley and Dr. Rafael V. Davalos of Virginia Tech. The procedure is now being carried out around the world and according to Dr. Laura Croccetti of the University of Pisa, an expert in ablative techniques, IRE's appeal lies in the numerous advantages it holds.

Non thermal and not drug-dependant
IRE's use of electricity as a means of ablation makes it a non-thermal alternative to other ablative techniques such as Radiofrequency Ablation and Cryoablation. Its non-thermal nature allows for the safer treatment of select tumours, such as those close to nerves or blood vessels. According to Dr. Crocetti, the use of electricity and not heat means that ".. issues associated with perfusion-mediated tissue cooling or heating (a significant challenge with thermal methods) are not relevant." IRE is also not drug-dependant, which eliminates the risk caused by potentially dangerous adjuvant drugs.

No damage to blood vessels, nerves and connective tissue
The procedure only causes damage to the cell membrane of the cancerous lesion, leaving other structures such as blood vessels (including microvasculature), nerves, and connective tissue intact. This helps quickly generate new healthy cells, speeds up the post-procedural recovery time and in Dr. Croccetti's opinion "... could greatly improve the clinical application of local ablation."

Highly focused
IRE can also be used in a highly focused and precise manner and Dr. Crocetti maintains that it "…creates a sharp boundary between the treated and untreated area in vivo. This would suggest that IRE has the ability to sharply delineate the treatment area from the non-treated, and that treatment planning can be precisely performed according to mathematical predictions."

Minimally invasive and quick
IRE can be carried out percutaneously by an interventional radiologist, through a small nick in the patient's skin. This minimises the impact the procedure has on the patient and shortens the hospital stay time, with some patients being free to leave on the day of the procedure. The procedure time itself is also shorter than for other ablative techniques and as Dr. Crocetti explains "IRE can effectively create tissue death in micro- to millisecond ranges of treatment time compared to thermal ablation techniques, which require at least 20 minutes to hours."

The NanoKnife IRE System®

Numerous positive pre-clinical trials on IRE led the American Food and Drug Administration (FDA) to clear it for use in the ablation of soft tissues cancers in November 2006. Following the clearance by the FDA, the company Angiodynamics was the first to release a device - NanoKnife IRE System® - which uses IRE to safely and effectively ablate cancerous soft tissue cells. Prof. Thomas Helmberger, an interventional oncological specialist who has used the device, describes it as "an electroporation system consisting of a high voltage generator controlling voltage, pulse length, pulse intervals, and probes for delivering energy into the tissue."

© AngioDynamics

How does the NanoKnife IRE System® work?

1. Before the procedure is carried out, ultrasound or CT is used to determine the size and location of the cancerous lesion.
2. A small nick is made in the skin, through which small electrodes are placed in or sandwiched around the lesion under image-guidance.
3. The electrodes deliver a series of short, intense electrical pulses to the lesion. The precise distance between the electrodes and the strength of the electrical pulses are carefully calculated prior to the procedure.
4. The targeted cancerous area dies naturally almost instantly, but vital structures such as blood vessels and nerves are left intact, as well as normal surrounding tissue.
5. Once the cancerous tissue is dead, it is progressively absorbed by the surrounding tissue.

IRE today

IRE is now being used in centres around the world, and Prof. Helmberger points out that ".. a few hundred procedures have already been performed under research conditions". Although the "data available so far suggest that IRE is not related to increased risk compared to any other percutaneous procedure", Dr. Crocetti maintains that "more clinical data is needed to assess the safety profile of the technique." Numerous studies are underway to assess the safety of the procedure, including a multi-centre trial in which Dr. Croccetti is involved. The European trial, which is being coordinated by the renowned physicians Prof. Riccardo Lencioni (IR) and Prof. Jordi Bruix (Hepatologist), will include seven centres in Italy, France, Germany and Spain. Dr. Crocetti describes the trial as being ".. aimed at evaluating the safety and efficacy of IRE for the treatment of early-stage hepatocellular carcinoma. The enrollment has just started and we hope to produce the results very soon."

Conclusion

The non-thermal and highly focused nature of IRE makes it a useful tool for the treatment of cancerous tissues found close to blood vessels and nerves. In addition, IRE boasts numerous other advantages; it is quick to perform and minimally invasive. In the words of Prof. Helmberger "IRE seems to be one of the promising 'new kids on the block' of ablative therapies and the ongoing research will help elucidate its role within the armamentarium of interventional oncological therapies." When electricity was first used in everyday life, it revolutionised the way people lived. Now Irreversible Electroporation, though still in its starting phase, may revolutionise cancer care.

The Best of Both Worlds

How the patient benefits from specialist cooperation

Understanding what skills your colleague can offer is essential if your patient is to be given all the options available. With this in mind, ECIO 2010 launched an inspired new programme, "Bring Your Referring Oncologist", where IRs were offered the chance to bring their oncologist or hepatologist colleagues along to the congress.

IQ spoke to two such pairs of mixed colleagues who enjoy a successful professional relationship, to see why they had decided to take part, and what advice they would give to other interdisciplinary team members.

Dr. Magdalena Kiczynska is an oncology resident at the Medical University of Lublin, Poland. She attended ECIO in partnership with the Head of the Interventional Radiology Department, Prof. Małgorzata Szczerbo-Trojanowska.

University of Lublin, Poland. Image reproduced by kind permission of the Medical University of Lublin

Dr. Kiczynska, why have you decided to come to ECIO? What role can IR play for cancer patients?

"As an oncology resident, I am really interested in all treatment options for patients. Liver tumours are my area of specialisation, and as our hospital offers many IR treatments for these tumours, I have been working quite closely with this department from the beginning of my residency.
My decision to attend this meeting is quite a simple one – it is an interventional radiology congress, but also an oncology congress, and so is relevant to all who work in this field. The treatment options discussed here are treatments the patients in our department undergo, and it is important that we understand the procedures themselves, and the correct indications for them. Our own cooperation with the Department of Interventional Radiology allows our patients many additional opportunities for treatment, which, of course, is highly beneficial."

Prof. Szczerbo-Trojanowska, how has collaboration between the IR and Oncology Departments come about?

"The close collaboration between the IR Department and the Oncology Department is a long-standing one – even before these current curative options were developed, our IR Department was treating patients using palliative techniques, such as embolisation in renal tumours and lung cancers, or catheter drainage, so our oncologists have great awareness of the possibilities that IR raises for patients. This mutual relationship has obviously evolved alongside IR itself, and these days we work together frequently on chemoembolisation."

Prof. Małgorzata Szczerbo-Trojanowska & Dr. Magdalena Kiczynska

Prof. Szczerbo-Trojanowska, how is this collaboration maintained from day to day?

"A member of the IR team usually attends the daily clinical discussion of patients, and if IR treatment is considered an option, we give our proposals. Not every patient can undergo these procedures, so it's important that we discuss it jointly, rather than just performing on request from our non-IR colleagues.

Magda [Kiczynska] is also very much involved in the procedure itself, so she is always with the patient in our department, following every procedure, which makes it much more comfortable for the patient. The patient gains reassurance from knowing that the doctor who is in charge of them is always with him or her. Follow-up is another area of cooperation."

Dr. Kiczynska, how are IRs involved in after-care of cancer patients?

"We in the oncology department monitor the patients following treatment, and report the results to our IR colleagues. It's important that they are aware of the early results, whether there seems to be post-embolisation syndrome or not, or if there is a need for a second session, and so on."

Dr. Kiczynska, would you recommend that your oncological colleagues attend the next ECIO meeting?

"I'm delighted to be at ECIO – to invite all specialities involved in the treatment procedure to a joint educational meeting is a brilliant idea. It's especially valuable for the patient, because it is in their best interests that all the doctors who have contact with him or her can share knowledge of their specialities and their work."

Dr. Eva Horndasch & Prof. Dierk Vorwerk

Dr. Eva Horndasch is an oncologist at Klinikum Ingolstadt, Germany. She works in close partnership with her colleague, Prof. Dierk Vorwerk, who is an interventional radiologist at the same hospital, as well as being Editor-in-Chief of the medical journal CardioVascular and Interventional Radiology.

Dr. Horndasch, how is a patient's treatment path decided in your hospital?

"At Klinikum Ingolstadt, we have regular multidisciplinary tumour boards - at least one a day - dealing with different tumours types. In these meetings we discuss, among other things, if a case is something for the IR, is it for the surgeon or is it purely for the oncologist?"

Prof. Vorwerk, what areas is IR currently making the greatest contribution in your hospital?

"With HCCs or Hepatocellular Carcinomas, for example, embolisation is now established and is always considered. With benign tumours, a lot has changed and IR is being used more, for example with embolisation of uterine fibroids. Things have certainly come a long way in the last few years, and it's exciting to think where the discipline will be 5 years from now."

Dr. Horndasch, what needs to be done to improve awareness of IR options?

"From my perspective, I think that it needs to be made clearer that these options exist. I think not enough emphasis is put on interventional radiology techniques. IRs have great treatments to offer: they need to be more confident in saying 'we have options and we are ready to provide them'.

I feel that the problem also lies with us oncologists, who don't include ablation sessions in most oncological congresses. When I look back on the past congresses that I have attended, the focus was often firmly placed on chemotherapy, less on surgery, and with hardly anything on ablation. This is a great pity, and one of the reasons that ECIO is a valuable opportunity for oncologists to learn about these possibilities."

Prof. Vorwerk, what are your recommendations for improving patient access to IR?

"We have some good data on ablation, but what we really need is data on combined therapy, because very few patients get ablation or surgery in isolation - they get a combination of treatments. That is where we need more research and data, especially on which patients are most suited for combined therapies, such as chemotherapy and ablation.
We have treated some patients with combined ablation and chemotherapy and they recovered well, much better than they would have with one of the treatments alone. But scientific data is missing to support this, and patients are treated according to a protocol, where ablation therapies are always at the end of the chain. Only patients who don't respond well to other therapies are offered ablation. This leads to biased information due to the poor selection of patients and the chances of recovery are very slim. This is one area we need to concentrate on.

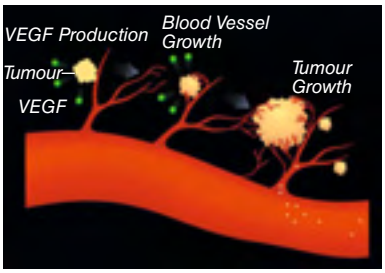
While many hospitals are introducing multidisciplinary boards, it is not yet typical, at least not in my opinion, for all specialists involved to ask themselves the question 'can this be treated with ablation?' The answer will sometimes be yes, and sometimes no – but it is important that the question is asked. We're working hard to raise that awareness, with the help of our non-IR colleagues like Dr. Horndasch, and I believe we are making good progress."

Klinikum Ingolstadt, Germany

Targeted Therapy
The Short Circuit for Cancer

Looking back to our school years, some of us may recall a physics lesson we once had on electricity. We may still remember the teacher describing how circuits work and how certain materials could hinder surges of electricity from passing through them.

Maybe the thought of that old physics lesson brings back happy memories of childhood curiosity or sad memories of how you failed that physics test. Nevertheless, the lessons you learned that day can be used to illustrate a novel method of cancer treatment called Targeted Therapy (TT).



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What is Targeted Therapy (TT)?

Cancer cells, like all living cells, have a series of signal pathways (like circuits) which are responsible for maintaining the viability of the cell. Examples of the signals sent include those that allow cancer cells to divide uncontrollably or signals that protect them from natural cell death.

Targeted Therapies (TT) damage or kill cancer cells by interfering with these signal pathways. This is done by blocking "molecular targets" which are the molecules that act as "conductors" or "light switches" in the pathways. Once these molecules are impeded, the circuit is broken, damaging the cancerous cells. Vast numbers of molecular targets exist, many of which have yet to be fully understood. They include certain forms of enzymes, growth factor receptors and genes.

TTs vary greatly depending on the molecular target they are impeding and numerous TT drugs have already been approved for cancer treatment in a range of countries. IRs are also playing an important role in this revolutionary form of treatment, especially in the areas of "Angiogenesis" and "Tumour Metabolism".

Angiogenesis

Angiogenesis is the natural physiological process by which new blood vessels grow from existing ones. Should the need for a new blood vessel arise, then angiogenetic activators prompt blood vessel growth. Normal angiogenesis is vital for the growth and development of cells as well as for their regeneration following injury (e.g. wound healing).

> IRs are playing an important role in this revolutionary form of treatment, especially in the areas of "Angiogenesis" and "Tumour Metabolism"

Angiogenesis is vital to cancer cells, as without an adequate blood supply, tumours cannot grow beyond 1-2 mm. Blood flow provides the cancer cells with nutrients and helps remove the large amount of waste they produce. It also allows the cells to be transported in the blood stream and become lodged in other parts of the body - a process known as metastasis. Cancer cells abnormally release angiogenetic activators such as vascular endothelial growth factor *(VEGF)* and basic fibroblast growth factor *(bFGF)*, thus forming signal pathways that ensure they have a good blood supply.

Anti-angiogenetic Therapy (as opposed to pro-angiogenetic therapy which is being explored for use in cardiovascular diseases) aims to interfere with the signal pathways that lead to the formation of new blood vessels in cancer cells. Anti-angiogenetic drugs are already being used to treat various forms of cancer including those of the kidney, certain gastrointestinal cancers, and an aggressive form of brain cancer called glioblastoma.

Hope for Glioblastoma Patients

Glioblastoma is one of the most common forms of brain cancer in humans and gives rise to adverse symptoms such as intense headaches, seizures and nausea. As with other forms of brain cancer, the prognosis for Glioblastoma patients is poor due to the complexity of neurological interventions.

An advanced TT is being used to offer glioblastoma patients new hope. The anti-angiogenetic drug Avastin (Bevacizumab) can be administered, intra-arterially and under image-guidance, directly to the brain tumour. Once administered, the drug works by binding to the growth factor (VEGF), thus interfering with its signal for the production of blood vessels. In this way, the tumour is essentially starved of nutrients and subsequently killed.

Tumour Metabolism

Another process that is fundamental to the viability of cancer cells is a process known as tumour metabolism. Metabolism describes a set of signal pathways which help living organisms maintain life and include signals that cause cells to grow, reproduce and maintain their structures. A key part of metabolism, both for normal cells and for tumour cells, is energy production.

Cancer cells require much more energy than normal cells to remain viable. A key element in energy production in normal cells is oxygen - something that cancer cells often lack due to their poor infrastructure. In 1931, the German scientist and Nobel Laureate Otto Warburg discovered the key to how cancer cells produce their energy from glucose despite their lack of oxygen. His findings laid the foundation for the discovery of a target molecule that could interfere with the signals released during tumour metabolism, thus cutting off the cancer cell's energy supply, subsequently damaging them.

Inhibiting Energy Production

A novel TT that targets tumour metabolism is the glycolysis inhibitor 3-Bromopyruvate (3-BrPA) which can be administered intra-arterially by an interventional radiologist. The drug works by interfering with the signal pathways of the cancer cells that convert glucose into energy. Intracellular energy is thus depleted and cell death occurs.

Targeted Therapies are right at the forefront of modern medical advances and IRs are playing their part. They give us a preview of a time in which patients' treatment plans may be "hand-picked" for them based on the "molecular targets" which are present in each specific form of cancer. By focusing on specific targets, TTs may also prove to be less harmful to normal cells than conventional therapies such as chemotherapy. However, the treatment is still very much in its infancy and certain problems are still to be solved, such as the build-up of cell resistance to certain drugs over time. However, as TT develops, new targets will undoubtedly be found, providing us with many more ways to short circuit cancer's signals for good.

By focusing on specific targets, TTs may prove to be less harmful to normal cells than conventional therapies such as chemotherapy

Interventional Oncology Featured Trial

A Phase II Randomized, Double-blind, Placebo-controlled Study of Sorafenib or Placebo in Combination With Transarterial Chemoembolization (TACE) Performed With DC Bead and Doxorubicin for Intermediate Stage Hepatocellular Carcinoma (HCC)

Transarterial Chemoembolisation (TACE) has been obtaining good results in treating primary liver tumours (HCC) for many years. These results were again improved with the relatively recent introduction of DC beads loaded with doxorubicin, which is now becoming widely used as a TACE agent.

Study Aims
This study aims to evaluate whether the progression of the disease can be slowed further by combining the doxorubicin-loaded beads with the molecule inhibitor sorafenib. In order to evaluate this, 300 HCC patients are being enrolled, and will be assigned either to a DC beads and sorafenib combination therapy, or a DC beads and placebo combination.

Study Design
The trial will be a double-blind randomised trial – neither patient, care giver nor investigator will be aware during the trial of which programme the patient has been assigned to. The primary outcome is to evaluate disease progression time under the two treatment arms:

- **Patients in Arm 1**, the experimental group, will be given 4x200mg sorafenib tablets daily (2 tablets twice daily), while also undergoing TACE using DC beads.
- **Patients in Arm 2**, the control group, will be given the same regiment, only with placebo tablets used instead of sorafenib (2 placebo tablets twice daily, accompanied by TACE using DC beads).

Recruitment
The study recruitment began in March 2009, and aims to be completed by May 2011. Its primary outcome data should be released in December 2010. A large number of centres worldwide are taking part, including centres in France, Germany, Italy, Austria, Spain, Belgium, USA, Canada, China, Korea, Taiwan, Singapore and Australia. Recruitment for the study is now closed.

The trial is being run under the auspices of Bayer Healthcare.

For more information, please contact:
Kate Hollis
Study Manager, Bayer Healthcare
Email: kate.hollis@bayerhealthcare.com
Telephone: +44 (0)1635 563240

Please read on for a selection of other Interventional Oncology Trials and Registries >

Amendment from IQ, Issue 1 Understanding Cancer, page 12

Yttrium-90 Radioembolisation

Used palliatively to treat primary and metastatic liver tumours, particularly good for multiple, scattered tumours. Suitable for use in both patients without cirrhosis, and those whose cirrhosis is not too advanced, as good liver function is required (e.g. Child-Pugh A or B).

Radioembolisation is another application of embolisation, but in this instance, it uses radioactive microspheres. The beads become lodged in the vessels feeding the tumour(s), and the radiation emitted causes cell death.

The radioactive isotope Yttrium-90 is used, as its penetration averages 2.5mm in tissues, meaning that the radiation only treats the tissue it is lodged in, and not the healthy surrounding tissue. This also means that a higher dosage of radiation can be given.

As this radiation is applied internally, it is also referred to as (selective) internal radiotherapy. It has relatively few side-effects, compared with standard treatments, with fatigue for seven to ten days following the procedure being the most common.

IQ apologises for any misunderstanding.

Interventional Oncology Trials and Registries

Trial: a study carried out with the purpose of testing a new medical treatment on a defined group of people. The results are compared with a group that are treated using another method and/or a control group.

Registry: a (retrospective) collection of data about a certain treatment or illness. Using the compiled data, conclusions can be drawn about effectiveness of a particular treatment method.

Microwave Ablation of Resectable Liver Tumors

Contact
Ms. Maria Gonzalez, St. Joseph Hospital of Orange, CA, US
Date opened
April 2009
Status of trial
Recruiting
Description
The purpose of the protocol is to pathologically evaluate the destruction by microwave ablation of primary and metastatic liver tumours. The primary aim is to measure tissue destruction with the MedWaves Microwave Ablation/ Coagulation Ablation System.
ClinicalTrials.gov Identifier: NCT00892255

Pilot Study of Irreversible Electroporation (IRE) to Treat Early-Stage Primary Liver Cancer (HCC)

Contact
Dr. Riccardo Lencioni, University of Pisa School of Medicine, Pisa, IT
Date opened
February 2010
Status of trial
Recruiting
Description
The purpose of the study is to evaluate the safety and efficacy of Irreversible Electroporation (IRE) for the treatment of early-stage Hepatocellular Carcinoma (HCC).
ClinicalTrials.gov Identifier: NCT01078415

IQ takes no responsibility for the content of the individual trials and registries; please refer to their source (www.clinicaltrials.gov) for further information.

Please note, this does not constitute an exhaustive over view of trials and registries. If you are aware of a trial or registry which may be of interest to our readers, please feel free to contact us at info@intervention-iq.org.

www.intervention-iq.org
www.clinicaltrials.gov
www.controlled-trials.com
www.who.int/trialsearch
clinicaltrials.mayo.edu

Radioembolization with Yttrium-90 Microspheres for Intermediate or Advanced Hepatocellular Carcinoma

Contact
Dr. Vincenzo Mazzaferro, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT
Date opened
July 2007
Status of trial
Recruiting
Description
The purpose of the prospective phase II study is to determine whether or not radioembolisation with Yttrium-90 microspheres (TheraSphere®) provides an anti-tumoural effect and a sensible benefit in terms of time-to-progression (TTP) and survival in patients with good liver function (Child A-B7) and a confirmed diagnosis of intermediate or advanced (due to the presence of neoplastic portal thrombosis) HCC.
ClinicalTrials.gov Identifier: NCT00910572

Radiofrequency Ablation, Chemoembolization, and/or Radioembolization in Treating Patients with Liver Cancer that cannot be Removed by Surgery

Contact
Dr. Riad Salem, Northwestern Memorial Hospital, IL, US
Date opened
August 2009
Status of trial
Recruiting
Description
The randomised phase II trial examines radioembolisation to see how well it works compared with chemoembolisation and/or radiofrequency ablation in treating patients with liver cancer that cannot be removed by surgery.
ClinicalTrials.gov Identifier: NCT00956930

Transarterial Chemoembolization versus Proton Beam Radiotherapy for the Treatment of Hepatocellular Carcinoma

Contact
Dr. Zeid Kayali, Loma Linda University Hospital, CA, US
Date opened
January 2009
Status of trial
Recruiting
Description
The first randomised trial in the medical field to compare head-to-head the efficacy of TACE versus proton beam in treating HCC patients. TACE is considered the most common locoregional treatment used to treat HCC. Proton beam radiotherapy has been used in treating HCC in a few centres across the globe with phase I and II trials showed satisfactory safety and efficacy results.
ClinicalTrials.gov Identifier: NCT00857805

IR Without Borders

Access in high income countries to interventional radiology and other modern medical care is continually improving. But how can we ensure that others outside our own comfort zone feel the benefits that innovative medical science has to offer?

As it stands, continual technological developments and rigorous safety guidelines cause many older, but still perfectly functioning, imaging machines to be replaced. While this has advantages for patients, it does mean that a lot of perfectly good equipment is left idle.

If you put these two problems side by side, a solution presents itself – why not send these extra machines to hospitals that could use them? This is the goal of several medical charities who aim to improve medical care in developing countries. Other charities seek financial donations to provide this equipment, or petition companies to donate it directly. However, while a sound idea in theory, it is, like all charitable aid, one that needs to be well thought out if it is to be effective.

In order to find out more, IQ spoke to Dutch radiologist, Dr. Elizabeth Joekes, who spent 3 years working in Komfo Anokye Teaching Hospital in Ghana.

"The 'recycling' of medical equipment for low resource countries is a true mine field. Only too often equipment is donated without proper research into the local needs and facilities. Good quality ultrasound equipment is very useful at basic healthcare level, but training of the end users needs to be included and is often a problem. Basic X-ray systems can also be very useful, but need appropriate safety precautions, trained local radiography staff and local engineers for maintenance. Larger hospitals will benefit from fluoroscopy units and CT scanners. In all cases, proper needs assessment should be performed in advance and local healthcare staff involved in the decision."

Aside from training, there are many other practical considerations:

"The logistics and finances usually depend on charities, volunteers from Radiological Societies or individual initiatives. Several companies sell refurbished second-hand equipment and transport companies usually offer special rates for medical freight. Dismantling, transporting and installing the equipment can be more costly than expected and passing the goods through customs can often incur large import duties. Taking all this into account, the costs of sending donated equipment may still be far more than the local government or hospital can afford and should be weighed up carefully against the expected benefits. Unfortunately, investing large sums of money in equipment that stands idle most of the time is a common waste of scarce resources."

Dr. Elizabeth Joekes

One of the most pressing concerns is that of patient safety:

"Sadly, equipment safety is a big problem and a lot of the equipment is not maintained or monitored at all. A lack of appropriately trained staff and engineering support is the norm in a large number of places. The donation or purchase of equipment without appropriate training and sustained maintenance is in large part responsible for this situation and puts many patients and members of staff at risk."

[Accordingly, ultrasound can often be the most beneficial addition to an under-funded hospital's armoury, and is something charities such as GUEDF (Global Ultrasound Equipment Donation Foundation) actively promote – the modality is not only affordable, it is also easier to implement and maintain than conventional x-rays and does not emit radiation. However, much harm can be caused if it is improperly used and safety training is crucial for the protection of patients and medical staff.]

Dr. Joekes explains what IR procedures can be carried out under ultrasound-guidance:

"Procedures such as abscess and effusion drainages are very beneficial in developing countries with high rates of infectious diseases. Nephrostomies and even percutaneous biliary drainages can be performed with ultrasound alone. In general, biopsies will be less useful, unless facilities for histology and cytology are also available."

Many of the most well-known IR procedures deal with what one could call "western" diseases, or conditions associated with the elderly, such as various cardiovascular diseases. However, IR is a versatile discipline, and has many applications in less affluent communities too:

"Dealing with the complications of infectious diseases and

A Doctor performing ultrasound

Entrance of the Komfo Anoky Teaching Hospital

trauma are the areas where IR can have a major impact. Drainage procedures are cheap, simple and can save lives, for example in relieving an obstructed infected kidney. In many cases, surgery can be prevented. This is significant, as in many countries surgeries have a high risk of complications, related to sepsis and a lack of pre- and post-operative support facilities.

"More sophisticated interventional techniques could be helpful in larger centres, e.g. gelfoam embolisation of traumatic haemorrhage or post-partum haemorrhage, and intra-arterial and percutaneous treatment of liver cancers. The latter are very common in many developing countries and often occur in young adults supporting large families. Life extension, if not cure, can make a huge difference. Unfortunately, the cost of these procedures is prohibitive for most patients at present.

"At Komfo Anokye Hospital, drainages and biopsies are performed on a daily basis now. Nephrostomies are common and biliary drainages incidental. A fluoroscopy unit with angiographic facilities is available, but consumables are very difficult to import, due to company regulations related to traceability and billing."

Acquisition of consumables is not the only area that needs improving if availability of IR is to be ensured:

"Improving access to IR will also require large investments in ultrasound training programmes and basic interventional training. Although grants for visiting fellowships to the "West" are a major step forward, it would be more relevant to the practice in developing country hospitals to support experienced IR practitioners to visit those hospitals and assist local staff in setting up a programme. This will foster long-term links and develop skills which are locally relevant, but will also require long-term visits and considerable commitment from IR practitioners and their departments at their base hospital. Unfortunately, many potential teachers do not find the opportunity for such longer term commitments."

Dr. Joekes, however, decided to apply for a local post as consultant radiologist at Komfo Anokye Teaching Hospital in Ghana, and is proud of her achievements there:

The Vitals

Dr. Elizabeth Joekes is a Dutch radiologist with a strong IR background. As a medical student and junior doctor, she spent several short periods of time in Africa, volunteering and later teaching ultrasound. She worked for three years at a training hospital in Ghana, before taking up a post in Liverpool, UK, where she is mostly involved with infectious diseases and GI radiology. In addition, she teaches radiology for developing countries at the Liverpool School of Tropical Medicine and is involved in several radiology-related research projects in developing countries.

"After three years, the department had grown considerably, with new registrars joining and two local radiologists taking over. The promotion of radiology as a respected and useful specialty, with local staff providing the next generation of radiologists is a major improvement. Reorganising workflow increased patient access, with ultrasound numbers quadrupling in those three years. Introducing IR procedures on a small scale also changed management for many patients."

Following this positive experience, Dr. Joekes would encourage everyone to consider taking a post in an "unusual" place.

"Ghana and other developing countries are not the alien, faraway places we so often perceive them to be, but places which are in large part very similar to our own and where interesting jobs can and need to be done - places where our contribution often has a much greater impact than in our home countries and where we can challenge many of our own ideas. Learning to live and work in a different culture is an unbeatable, life enhancing experience in which the benefits far outweigh the "bravery" required. I would encourage anyone interested in contributing to the development of radiology and IR in developing countries to create that opportunity and discover that it is a very rewarding experience and not half as hard as it seems."

The Global Statement Defining IR

IBM and General Electric have one, so does Coca Cola, and even Walt Disney. Most leading companies today could not do without having their own mission statement. The statement poses as a form of "creed" in which the core elements of that organisation are recorded and key questions are answered - who are we, what do we do, and where are we headed?

Mission statements are not only restricted to organisations and companies - certain medical specialities have them too. While the benefits of an organisation or company having a mission statement are clear, what good could such a statement bring for a medical specialty? In IR's case it would provide a unified and accurate picture of the discipline in a more accessible format. This is particularly important as many patients are still not being offered the benefits of IR's minimally invasive treatments because of a lack of awareness of the discipline.

In the 2008 annual meeting of the Cardiovascular and Interventional Radiological Society of Europe (CIRSE), a group of IR experts, led by then society Presidents Jim Reekers (CIRSE) and John Kaufman (SIR, Society of Interventional Radiology, US), set out to create a form of mission statement for IR. The result was the "Global Statement Defining Interventional Radiology" which was published in the August 2010 issues of the journal Cardiovascular and Interventional Radiology (CVIR) and the Journal of Vascular and Interventional Radiology (JVIR). Endorsed by 42 societies in 39 countries, the Statement not only provides a concise definition of the discipline, it also stands as proof of IR's international importance.

Statement excerpt

In each country and region, IR practice varies according to local factors... The following features are common to ... IR:

1. Expertise in diagnostic imaging and radiation safety
2. Expertise in image-guided minimally invasive procedures and techniques as applied to multiple diseases and organs
3. Expertise in the evaluation and management of patients suitable for the image-guided interventions included in the scope of IR practice.
4. Continual invention and innovation of new techniques, devices, and procedures.

Based on these features, IR is unique and distinct from all other surgical, radiologic and medical subspecialties and specialties.

Sections of the Statement

Defining a multi-faceted discipline like IR in a few pages is not an easy task, especially as the status of the discipline often differs from country to country. The Global Statement does not set out to offer an unnecessary, falsely homogenous view of IR but chooses instead to highlight the common elements that unite the discipline around the world. The Statement comprises of sections, each dealing with a separate element of IR:

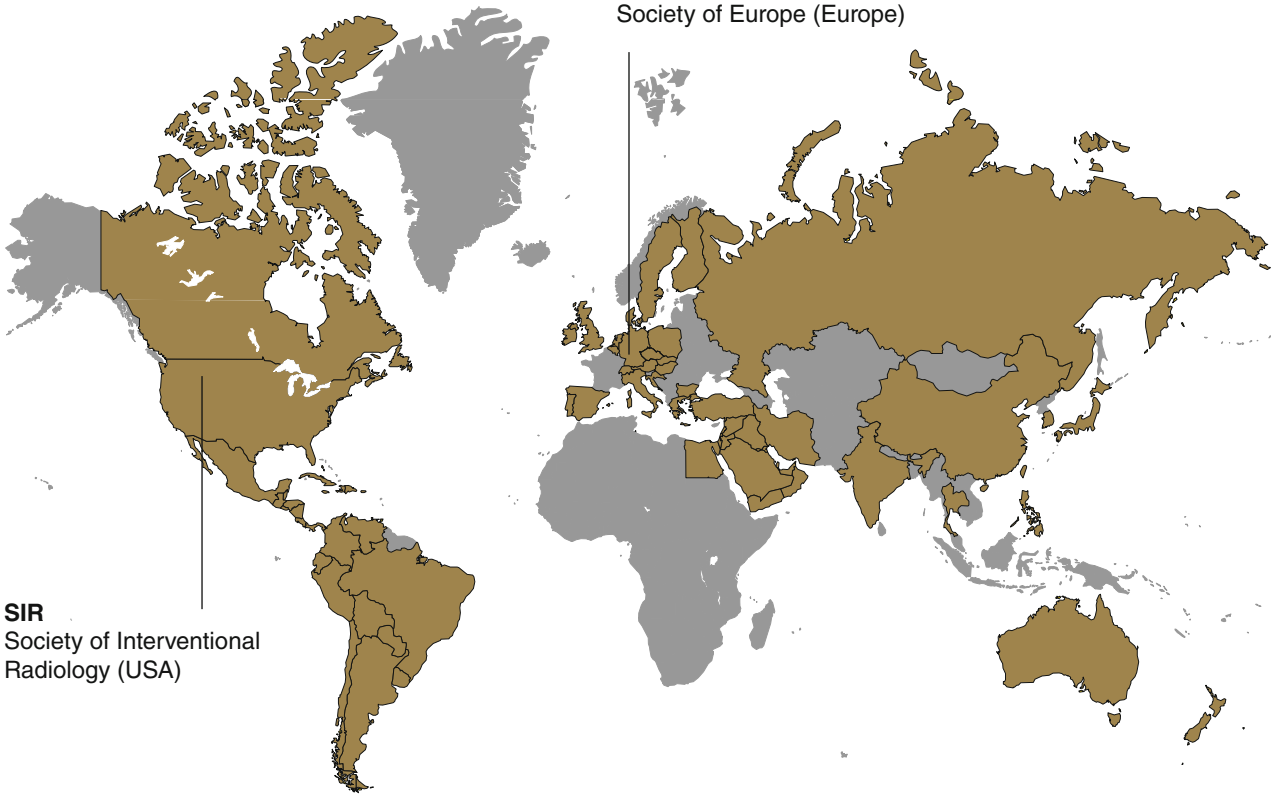
"Clinical Scope"
This section of the Statement describes IR's multi-faceted nature, listing the body-systems which IR can be used to diagnose or treat. The impressive list includes: "...vascular, gastrointestinal, hepatobiliary, genitourinary, pulmonary, musculoskeletal, and, in some countries, neurologic conditions..."

"Training"
Part of IR's uniqueness is derived from the use of both diagnostic and interventional radiological techniques, with practitioners requiring training in both areas. Regulated training programmes are, therefore, of great importance for IRs around the world and the Statement lays down key characteristics that are required for proper training including instruction in areas such as radiation physics and radiation safety as well as longitudinal in- and outpatient care.

"Certification"
The introduction of the European Board of Interventional Radiology (EBIR) was a key milestone in the history of international IR certification. The Statement acknowledges the value of standardised certification in IR and also states the importance of continued medical education by requiring the "Maintenance of certification as required by national and local medical certifying bodies."

"Clinical Practice"
Interventional radiologists are not only technical experts, they are also clinical practitioners. This section emphasises the importance of having dedicated staff and resources allocated to IRs in order to maintain good clinical practice.

"Quality"
The complexity of the procedures carried out by IRs requires precision and the adherence to best practice guidelines. IRs are called to pledge a "life-long dedication to continuous quality improvement," and to adhere to "... official IR societal practice standards whenever feasible."



"Research"
IR is based on the use of cutting-edge technology to treat an array of illnesses. Research is integral to the development of these technologies and, in this way, also to the development of the discipline. The section on research underlines the significance of this work and encourages IRs to further investigate "..diseases and conditions treated with image-guided techniques," and develop "new image-guided interventional techniques and devices."

"Professionalism"
Patients benefit most when physicians from various specialties are able to pool their knowledge and skills to find the best possible form and course of treatment for them. The Statement highlights the interventional radiologist as a team player for the benefit of the patient. Other elements which should be common practice for a professional IR are also listed in this section including the open disclosure of conflicts of interest and the promotion of IR as a first treatment option whenever appropriate.

Conclusion

The main aim of the authors of the Statement was to create a document that accurately defined the discipline in a way that could be easily communicated to others. This could, in turn, be used to raise awareness about IR and counter the cases in which potentially suitable patients are not offered IR as a treatment option. With the Statement written and approved by IRs around the world, the next step would be its appropriate circulation. Since its release, the Statement has made its way into awareness campaigns, publications and journals across the globe, spreading a unified message about IR.

For more information on the Global Statement Defining IR, please contact ugbor@cirse.org.

IR in Veterinary Medicine

You know an idea is a good one when it spreads even further than it was originally intended to, and that's exactly what is happening with IR. The results that IRs are obtaining in their patients has caused another profession to follow suit, leading to a whole new field – minimally invasive veterinary medicine.

Although this is a relatively new discipline within veterinary medicine, the clinics that offer it are already experiencing high demand. The reasons are obvious – if there is a procedure available that can reduce the need for hospitalisation, anaesthesia and invasive surgery, why not offer it to our smallest and fluffiest patients too?

No one told Benji he wasn't supposed to eat sticks! © Monika Wisniewska

Tailoring IR

Of course, it's not as straightforward as simply doing a procedure that's designed for the human body in a dog or a cat. Animals have their own anatomical structures, peculiarities and disease tendencies, and vets have had to put time and effort into adapting IR techniques to suit the anatomy of their four-legged clients. Materials are another barrier to be overcome – an adult human is bigger than a chihuahua, so the stents and catheters available are going to be too big. In such a new and small market, vets can have trouble finding the right size of instrument for their miniature patients.

Nonetheless, there are a number of techniques that are widely used within this infant field. Most of these are performed under fluoroscopy guidance – needless to say, imaging equipment is a prerequisite for doing these technically challenging procedures, and catheters, guidewires, balloons, stents, and occlusive devices are used to implement them.

Tracheal stenting
The most common of these is the use of stents to counter tracheal collapse. This is a common affliction of small dogs, where the airway that leads to the dog's lungs folds in on itself, making it difficult to breathe, and often first identified by persistent coughing. When this cannot be treated using medication, surgical placement of prosthetic rings around the trachea is the standard treatment. However, this is invasive and is associated with a high number of complications. Veterinary IRs (VIRs) can reduce this risk by placing stents (mesh scaffolds) directly into the trachea to hold it open. This procedure takes just 30 minutes, and the patient can be discharged after 24 hours. Complications are rare, but may include inflammatory tissue formation at the end of the stent, which usually responds well to steroid management.

Portosystemic Shunt
In a well-functioning liver, blood flows in from the portal vein and hepatic arteries, where (among other things) it is detoxified and sent back to the circulatory system via the hepatic veins. However, abnormal paths can exist, known as portosystemic shunts, which can move blood directly from the feeding vessels to the hepatic veins, bypassing the liver entirely and causing unpleasant symptoms. In small dogs, this abnormal connection is usually outside the liver, and can be effectively treated with surgery, but in larger dogs, it usually occurs within the liver, making surgical access difficult and dangerous. This type of shunt can be repaired by VIRs by means of embolic coils, which are delivered by catheter to partially block the abnormal connection, and are held in place by a perpendicularly placed stent at each end of the shunt. This allows the blood flow to return to normal, with sufficient blood being sent through the liver, stimulating liver growth.

Nutritional Support
It is not unknown for pets to contract illnesses that prevent them from eating normally, with severe vomiting and gastric motility problems preventing the animal from absorbing any nutrients. A temporary measure that can allow the animal to receive nutrients while their underlying condition is being resolved is nasojejunal tube placement. The most successful application of this treatment involves navigating a guidewire and catheter through the nose, down the throat and through the stomach and directly into the jejumum (small intestine), and then replacing the catheter with a feeding tube. Food can then be pumped directly into the animal's intestine, bypassing the problem areas of mouth and stomach.

© Simone van den Berg

Oncology
Humans aren't the only ones who can get cancers, and certain dog breeds are predisposed to certain cancers, such as bone cancer in Irish wolf hounds. Interventional oncology treatments similar to those used in humans are being developed, but are not yet at a stage where they are widely used, or even recommended. Treatments that have been used include embolisation (using glues and chemoembolic particles), radiofrequency and laser ablation and intra-arterial chemotherapy (see pages 6-9).

Foreign Body Retrieval
Animals, in their innocence, often do highly inadvisable things, like chewing on toys or small particles that can become lodged in their digestive tract or windpipe. Accidentally inhaled particles can range in size from seed-like to as big as a grape, while toys and bones are included in the "commonly eaten by accident" category. Such objects not only cause great discomfort to the animal, but can also damage the lining of the digestive tract as they work their way through. VIRs have developed foreign body retrieval techniques to remove such particles, feeding an aspiration catheter in through the mouth to the site of the object and gently removing it that way. Vascular retrieval techniques are used to remove any stents that have become dislodged or any catheter fragments from previous procedures.

Urinary Treatments
Underlying conditions can cause disruption to the urinary tract. If the urethers become obstructed, urine cannot easily leave the bladder, which can cause major discomfort and kidney problems. To rectify these blockages, VIRs can place ureteral stents or nephrostomy tubes to hold the ducts open, or can place a catheter that will act as a bypass, diverting the urine. Catheter drainage techniques can also be used to treat other undesirable fluid accumulations, such as cysts, abcesses and blocked bile ducts.

Step by Step

These procedures are proving popular where they are available, but there is a distinct lack of vets offering this service. This is due to limited training facilities – and proper training is essential if these procedures are to be carried out safely and effectively. Currently, there are only two institutes offering formalised training in the US (Michigan State University and the University of Pennsylvania), and few in Europe. As these procedures prove themselves to be safe and popular, however, more universities may start offering this training as part of their veterinary programme.

While vets may be dissuaded from getting involved in this field by the high start-up costs (for the imaging equipment), these techniques can be cost-effective in the long-run. Procedures can be done with shorter anaesthesia times, shorter hospital stay, and lower mortality than traditional surgical solutions.

IR is offering many therapeutic possibilities for domestic pets such as cats and dogs, and has also been used in more exotic animals, such as race horses, gorillas and rodents (more to follow in Issue 4). It's an exciting new step for veterinary medicine, and an exciting new sphere for IR, offering benefits to vets, pets, and all who love them.

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Trials and Registries

Trial: a study carried out with the purpose of testing a new medical treatment on a defined group of people. The results are compared with a group that are treated using another method and/or a control group.

Registry: a (retrospective) collection of data about a certain treatment or illness. Using the compiled data, conclusions can be drawn about effectiveness of a particular treatment method.

Angioplasty

Drug Eluting Balloon Angioplasty for Dialysis Access Treatment

Contact
Dr. Dimitrios Siablis, Patras University Hospital, Achaias, GR
Date opened
March 2010
Status
Recruiting

Description
The aim of the study is to compare the feasibility and effectiveness, by means of immediate and long-term results, of Drug Eluting Balloon (DEB) versus conventional balloon angioplasty for the treatment of failing dialysis access.
ClinicalTrials.gov Identifier: NCT01174472

Study Comparing Two Methods of Expanding Stents Placed in Legs of Diabetics with Peripheral Vascular Disease (COBRA)

Contact
Dr. Subhash Banerjee, Dallas Veterans Hospital, TX, US
Date opened
November, 2008
Status
Recruiting

Description
A trial in which investigators examine their hypothesis that cryoplasty, by inducing an apoptotic smooth muscle cell response, when applied to post-dilation of nitinol self-expanding stents in the Superficial Femoral Artery (SFA) of diabetics, would lead to decreased in-stent restenosis due to decreased neointimal proliferation.
ClinicalTrials.gov Identifier: NCT00827853

www.intervention-iq.org
www.clinicaltrials.gov
www.controlled-trials.com
www.who.int/trialsearch
clinicaltrials.mayo.edu

Embolectomy

Merci Registry - Real World Use of the Merci Retrieval System in Acute Ischemic Stroke

Contact
Concentric Medical, Mountain View, CA, US
Date opened
June 2007
Status
Completed, data to follow

Description
Post-market registry on the use of the Merci Retrieval System. Primary data collected include: post-procedure revascularisation success, 90-day mRS 0-2 and 90-day mortality.
ClinicalTrials.gov Identifier: NCT00478478

Embolisation

Effects of Carotid Stent Design on Cerebral Embolization

Contact
Dr. Carlos H Timaran, Dallas VA Medical Center, TX, US
Date opened
December, 2008
Status
Recruiting

Description
The goal of the study is to contrast the relative efficacy of closed-cell stents versus open-cell stents in preventing periprocedural cerebral embolisation in high-risk patients with symptomatic and asymptomatic extracranial carotid stenosis undergoing Carotid Artery Stenting (CAS).
ClinicalTrials.gov Identifier: NCT00830232

Neurovascular Embolization Cover for Treatment of Intracranial Aneurysms and Carotid/Vertebrobasilar Fistulae

Contact
Dr. Olav Jansen, Universitätsklinikum Schleswig-Holstein Campus Kiel Institut für Neuroradiologie, Kiel, DE
Date opened
October, 2008
Status
Recruiting

Description
The purpose of the study is to determine whether the NEC device can effectively occlude the intracranial aneurysm or the carotid/vertebrobasilar fistula and maintain parent vessel patency.
ClinicalTrials.gov Identifier: NCT01054391

Trans-Catheter Arterial Embolization and Surgery in Patients with Peptic Ulcer Bleeding Uncontrolled by Endoscopic Therapy (TAE)

Contact
Dr. James YW Lau, Chinese University of Hong Kong, HK
Date opened
April, 2007
Status
Recruiting

Description
The aim of the study is to compare the outcomes of Trans-catheter Arterial Embolisation (TAE) and surgery as salvage therapy of peptic ulcer bleeding after failed endoscopic therapy.
ClinicalTrials.gov Identifier: NCT00766961

Uterine Artery/Fibroid Embolisation (UAE/UFE)

A Prospective Study Comparing Contour SE™ Microspheres to Embosphere® Microspheres for Treating Symptomatic Uterine Fibroids with Uterine Fibroid Embolization (UFE)

Contact
Dr. Richard Shalansky-Goldberg, University of Pennsylvania, PA, US
Date opened
January 2006
Status
Ongoing, not recruiting

Description
The purpose of the study is to demonstrate comparability between Contour SE™ Microspheres and Embosphere® Microspheres for achieving post-UFE fibroid devascularisation in women with symptomatic uterine fibroids.
ClinicalTrials.gov Identifier: NCT00628901

Uterine Artery Embolization and Pelvic Floor Symptoms

Contact
Dr. Clifford Y Wai, University of Texas Southwestern Medical Center, TX, US
Date opened
January 2009
Status
Recruiting

Description
The objective of the study is to determine whether women who are already receiving treatment for their fibroids (i.e. UAE) demonstrate improvement in urinary symptoms and sexual dysfunction as well.
ClinicalTrials.gov Identifier: NCT00827645

Vertebroplasty/Kyphoplasty

Comparison of Balloon Kyphoplasty, Vertebroplasty and Conservative Management in Acute Osteoporotic Vertebral Fractures (OSTEO-6)

Contact
Dr. Jean-Denis Laredo, Hôpital Lariboisière, Paris, FR
Date opened
December 2007
Status
Recruiting

Description
The study aims to compare 3 treatments in recent (less than 6-week duration) non-traumatic (usually osteoporotic) vertebral fractures.
ClinicalTrials.gov Identifier: NCT00749060

KAVIAR Study - Kyphoplasty and Vertebroplasty in the Augmentation and Restoration of Vertebral Body Compression Fractures

Contact
Dr. Reginald Knight, Orthopedics International, WA, US
Date opened
August 2006
Status
Recruiting

Description
Patients with osteoporotic vertebral body compression fractures will be randomly assigned to treatment with balloon kyphoplasty or vertebroplasty. Over 2 years of follow-up, back pain, back function, quality of life, adverse events, subsequent fractures and cumulative healthcare costs will be compared.
ClinicalTrials.gov Identifier: NCT00323609

IQ takes no responsibility for the content of the individual trials and registries; please refer to their source (www.clinicaltrials.gov) for further information.

Please note, this does not constitute an exhaustive over view of trials and registries. If you are aware of a trial or registry which may be of interest to our readers, please feel free to contact us at info@intervention-iq.org.

The Early Days of IR

Professor Josef Rösch, IR pioneer, much published researcher and holder of multiple awards, tells IQ about his own early days in IR:

Josef Rösch
"An IR Pioneer"

- 1950, completed medical degree, Charles University, Prague, Czechoslovakia
- 1967, moved to the US
- Co-founder of the prestigious Dotter Interventional Institute in Portland, Oregon; Director from 1990-1993
- Awards include 4 gold medals, an endowed chair, an eponymous lecture and multiple lifetime achievement awards

In the early days, our work was quite different from what we do today. We were diagnostic angiographers and our goal was to define pathologic lesions so that referring physicians could select the proper therapy. Charles Dotter changed this mindset in June 1963 at the Czechoslovakian Radiologic Congress in Carlsbad, where he stated that the diagnostic catheter can become a therapeutic tool and replace the surgical scalpel. The audience was stunned. However, it took quite a while for us to change our diagnostic thinking and to develop interventional techniques and devices. The innovative IR pioneers concentrated on areas of their professional interests. My areas of interest were the abdominal organs and the gastrointestinal (GI) tract.

My horizons expanded when I arrived in Portland, Oregon in March 1967 for a one-year fellowship with Charles Dotter. Working with him and discussing his angioplasty cases was essential to my metamorphosis, and my approach to cases became more therapeutic. In 1968, I went from Portland to Los Angles for two years as visiting professor at UCLA. Timing was everything. I was in the right place, at the right time and with the right team. This combination was essential in developing my first interventional technique - selective vasoconstrictive infusions for treatment of acute arterial GI bleeding. After a promising experimental study, our young team successfully began to use this technique clinically. We sent our first results to the journal *Gastroenterology* and after a long delay, it was published with the sarcastic editorial comment "turn-off" bleeders. However, we were not discouraged and after successful experimental and clinical reports of Drs. Baum and Nusbaum, selective vasoconstrictive infusions became useful techniques in the early seventies for stopping both arterial and venous GI bleeding.

Our work on TIPS (transjugular intrahepatic portosystemic shunt) began in 1968. Inadvertent punctures of intrahepatic portal branches during transjugular cholangiography, used at that time at UCLA to define biliary obstructions, led us to explore this approach for visualisation of the portal venous system. These efforts, however, did not end with the introduction of just another diagnostic technique. Catalysed by Charles Dotter's conviction that any diagnostic catheter should be considered a potential therapeutic tool, we hypothesised that creation of an intrahepatic tract between the branches of the hepatic and portal veins could function as a portosystemic shunt, and sought to put this theory into action.

Pioneering team working on the creation of experimental TIPS. From L-R, J. Rösch, N. Ross, W. Hanafee, H. Snow.

It was not easy at that time to find catheters large enough to dilate a tract of sufficient size (18 French), but the West Coast Cook Medical representative, Mr. Ross Jennings, who later became vice president of Cook Group, Inc. helped provide them for us. By using 6 mm diameter tubing as a non-expandable stent, a substantial fraction of the portal blood was diverted into the systemic circulation and the shunt remained patent for as long as two weeks. Afterwards, however, clots began to form, and the shunts eventually thrombosed. This showed that although TIPS could be successfully created, occlusion was inevitable because tubing that was large enough to keep the shunt from thrombosing could not be placed percutaneously. So TIPS remained in the theoretical realm waiting for technology to catch up; which it finally did in the form of self-expanding metallic stents.

These techniques were based on experimental studies. However, when devising selective embolisation for treatment of arterial GI bleeding, "necessity was the mother of invention." When we could not stop bleeding from a gastric ulcer in a young patient with a blood clotting disorder, we selectively embolised the gastroduodenal artery with a blood clot and held it in place with vasoconstrictive infusions. This case, together with experimental studies, was the basis for the wide use of embolisation for treatment of arterial GI bleeding.

Present day interventionalists have a more defined clinical practice, with numerous established techniques, tools and devices to select from. Despite this, interventionalists should always be thinking about potential improvements in present procedures or developing new techniques. An innovative creative mind must be an integral part of every interventionalist.

Sincere thanks to Prof. Rösch, despite official retirement from clinical practice in 1995, is still active in research at the Dotter Interventional Institute.

What's in store

Coming up in Issue 4, April 2011

Women's Health

... The Quarter's Focus

If you are interested in contributing to IQ, please contact info@intervention-iq.org

Women's Health

How image-guided, minimally invasive therapy can help

Many gynaecological issues have traditionally been resolved with hysterectomy. While this has undoubtedly saved lives, it is nevertheless brutal, invasive surgery that leaves women unable to bear any more children. 30 years ago, interventional radiology began to help relieve this burden with the application of embolisation for post-partum haemorrhage – now the first choice treatment for this condition.

Inspired by success, IR began to treat other gynaecological complaints, and now offers safe, effective and minimally invasive options for potentially debilitating conditions such as uterine fibroids and pelvic congestion syndrome, and life-threatening conditions like invasive placenta. So join IQ as we explore the incredible involvement of IR in the lives of thousands of women worldwide, bringing them relief from their pain, fewer complications and, most importantly, hope.

Also featured:

- **The Changing Shape of Illness – how rising obesity creates new challenges for IR**
- **General Knowledge: what GPs know about IR**
- **Radiographer Training**

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