IR congress news

CIRSE 2009 - Lisbon
Tuesday, September 22, 2009

Josef Roesch Lecture

Michael D. Dake
CIRSE 2009 Josef Roesch Lecturer

The CIRSE Roesch Lecture was founded in 2003 in honour of Professor Josef Rösch whose award-winning research work spans more than 50 years, covering a wide range of Vascular and Interventional Radiology.
This year's Josef Roesch Lecture will be given by Michael Dake, Professor of Cardiothoracic Surgery and Director of the Catheterization and Angiography Laboratories at Stanford Medical Center.
Professor Dake has been heavily involved in research, particularly on endovascular device development, vascular biology and molecular imaging.
In 1996 Professor Dake was the first to treat a case of acute type B aortic dissection with a stent-graft. In 1999 he was the first author of an article in the New England Journal of Medicine providing the initial description of this procedure.

Don't miss it !
Josef Roesch Lecture
Today, 13:00
after CIRSE meets the EASD
Auditorium 1

CIRSE meets the European Association for the Study of Diabetes

CIRSE | EASD European Association for the Study of Diabetes

For years the number of people suffering from diabetes has been rising at alarming speed. According to the World Health Organisation, the number of patients with diabetes will double by 2030. Out of the numerous complications caused by diabetes, PVD is one of the most severe. It is estimated that it accounts for approximately 70% of all non-traumatic amputations.

Interventional radiologists have had a leading role in the treatment of PVD. CIRSE has therefore initiated cooperation with one of Europe's most active diabetes societies in Europe, the EASD, to work on ways the societies can contribute to improving the treatment of diabetes patients.

Today, 13:00, Auditorium 1

PROGRAMME

The diabetic foot in 2009 - an overview
A.J.M. Boulton
Medical aspects of peripheral vascular disease in diabetes
N. Schaper
Arterial bypass versus angioplasty in diabetic peripheral vascular disease
M. Lepäntalo

Julio Palmero da Cruz
Chairman of the CIRSE 2010
Local Host Committee

Dear Colleagues,

I feel very proud of and committed to the great task CIRSE has granted me of chairing the Local Host Committee for our 2010 meeting in my hometown of Valencia.

I am aware of the great responsibility that has been conveyed to me and I hope that together with my Co-Chairman and Committee I will be able to contribute to yet another great CIRSE congress, keeping up and hopefully even surpassing the level of our previous meetings. We know that this will not be easy, but we hope that together with a great, state-of-the-art and well-structured scientific programme and the beauty of our city of Valencia we hope to rise to the challenge.

The city of Valencia is located in the centre of Spain's Mediterranean coast and is well connected to the rest of Europe. Valencia is probably best known for its gastronomy, (most of all paellas), and the Fallas festival in which enormous statues depicting the vices and follies of mankind are displayed for a week and then burned in one night. It nicely symbolises various aspects of our culture – music, street life, passion, fire, creativity, humour and a great time.

Valencia has developed enormously in the last decade. Today it is a city well-known throughout the world for its sporting events, such as its Formula One races and the Americas Cup. The spectacular City of Sciences and Arts has made it a centre of modern architecture.

Despite the increase in attention Valencia has experienced, it has maintained its old charms. It is a big city, yet easy to get around in. It has a beautiful old town centre which reverberates with all the energy of the Mediterranean sun and the beach.

CIRSE 2010 will take place October 2-6, 2010 in the state-of-the-art compound Feria de Valencia. It is a modern and spacious, yet comfortable congress centre located 5km from the historic city centre and only a five minute drive from Valencia's international airport Manises. There are several bus lines connecting the congress venue with the city centre.

The Feria de Valencia will offer us 231,000 m² of exhibition space and 11,191 m² of lecture rooms, big enough to host 8,000 people. All this space will allow for a particularly comfortable congress atmosphere and an excellent industry exhibition, to which we owe greatly for its financial support.

We are very much looking forward to hosting another fantastic CIRSE meeting in Valencia. We know that CIRSE's great success and the growth it has experienced in recent years would not be possible without the work of the Executive Committee, the Central Office in Vienna and the Scientific Programme Planning Committee which is already working on offering another programme as comprehensive and interesting as always. It is this work that has contributed greatly to making Interventional Radiology one of the most attractive specialties with a high impact on patient care and the treatment of many diseases.

The Spanish Society of Interventional Radiology (SERVEI) who joined CIRSE as a Group Member will also do its best to contribute to the success of CIRSE 2010, providing its infrastructure and knowledge to CIRSE as part of the Local Host Committee. CIRSE 2010 will not only be an important international meeting, but also greatly further our specialty within Spain.

I look forward to welcoming you all in Valencia and will make sure that you will have an unforgettable time there!

CIRSE

Bayer HealthCare
Bayer Schering Pharma

Come Learn About Innovative Treatment Strategies for HCC

Bayer Schering Pharma Sponsored
Satellite Symposium

The Era of Systemic Therapy for the Treatment of Hepatocellular Carcinoma

Tuesday 22 September 2009
11:30 – 12:30
Auditorium 6, Centro de Congressos de Lisboa
Lisbon, Portugal

Chair:
Prof. Riccardo Lencioni, MD
Pisa University School of Medicine
Pisa, Italy

Faculty:
Thierry de Baere, MD
Institut Gustave-Roussy
Paris, France

Jeff Geschwind, MD
Johns Hopkins University
School of Medicine
Baltimore, United States

Bayer Schering Pharma AG, 13342 Berlin, Germany
www.bayerscheringpharma.de
EU.NEX.08-2009.0187

What's in the future for our specialty, what will we be doing in 10 years, and what can we look forward to? Anticipating the new frontiers in IR

Don't miss it !
Josef Roesch Lecture
Tuesday, September 22, 13:00-14:45
Auditorium 1

Michael Dake
Professor of Cardiothoracic Surgery
Director of the Catheterization and
Angiography Laboratories
Stanford Medical Center
Stanford, USA

Everyone wants to predict the future…to be able to anticipate the impact technology, economics and politics will have on our lives, our specialty and the practice of medicine. It is never easy, but those who can accurately envision the trajectories of progress and their complex interactions are in an enviable position to exert opportunistic influence on the course of events…and possibly to control the fates of history. So, what about us and IR; what does the future hold for our field? In some small, rarified corner of the universe, can we focus on reading the unwritten future chapters of our specialty; what lays ahead waiting for us to experience; which current practices will extinguish and what trends will be ignited over the next decade, and what will be important topics we will be discussing when we gather 10 years from now at CIRSE?

If we consider the three applied "disciplines" proven to exert profound forces on the practice of medicine, the one that is indelibly branded into the fabric of IR is technology. In some way it defines our role in the greater consortium of healthcare practitioners. It provides us with our splendid panoply of gadgets and tools that differentiate us and allow us to demonstrate our value to others. It allows us to consistently reinvent who we are and what we do in a manner that fosters creativity and sparks leading edge opportunities, and most of all, it propels us in pursuit of safer, less-invasive, more accurate, and effective alternative therapies that truly benefit patients. And after all, this is the promise of IR that attracted each of us. When it comes to the other powerful social sciences that leave significant historical impressions, economics and politics, the extent of their marks on the evolution of IR is less visible than the unique imprint of technology.

Consequently, because of the significant effect of technology and its sustained synergy with IR, it is in our collective interest to examine what the future may bring and brain-storm prospective scenarios we could encounter. Where to start? Hmmm, well how about here, right now? We are all currently experiencing a rapidly evolving technical revolution that dwarfs in magnitude the changes felt in earlier chronological periods in medicine.

These events are driven by a crescendo of multi-factorial forces that strikes IR from directions with coordinates scarcely recognized a decade ago—computational biology, genomics, proteomics, metabonomics, macromolecular imaging, nanoscience (nanomicroscopy, nanoparticles, etc.), cell trafficking, cell targeting, functional tracers and transporters, transgenic animal models, molecular pharmacology, biomarkers, bioinformatics, etc. This is not your father's catheter nor plain old balloon angioplasty or even your basic non-covered, non-drug eluting, non-bioresorbable stent. This is the future.

How will we take advantage of the dynamic recalibration of traditional medical priorities that will change the face of interventional therapies over the next decade? Let's explore some of the undeniable inevitabilities that are already apparent and ready to impact the practice of IR. We can already sense that the potential for dynamic functional monitoring of tissue metabolism looms large and will undoubtedly usher us into an era of more sophisticated image-guided therapy poised to replace procedures directed by simple structural anatomic rendering. In this context we will continue to experience increasing emphasis of patho-physiology over pathology, chemistry over physics and in vivo tissue observation over ex vivo tissue examination.

This will all lead to further development of algorithms designed to enhance the benefits of personalized medicine and exploit the advantages of prophylactic or preventative healthcare. We will continue to leverage the elemental power of molecular medicine as it displaces histology. As these new capabilities translate into clinical laboratories, we will soon participate in the integration of real-time multi-modality navigation; tracking and therapy monitoring that will supplant current practices of procedural planning based exclusively on imaging exams from prior encounters and only fluoroscopic end-point assessment.

Similarly, new paradigms will stress earlier point of intervention analysis of treatment efficacy that short-circuits the standard "wait and see" approaches to evaluating responses to therapy. This up tempo rhythm of diagnosis to therapy to re-assessment, conceivably all performed during the same encounter, is in accord with the accelerated rate of decision-making analysis that is now embedded in the patterns of care for patients with cancer, lymphoma, certain cardiac arrhythmias and selected neurological disorders.

These go-go clinical approaches will stress rapid bi-directional cycling between diagnostic and therapeutic phases supported by a similar research gyre or whorl between bench to bedside; basic to applied; pre-clinical to clinical and animal to human investigations. The deliverable goal is to step up the speed of innovation designed to generate meaningful outcomes of therapeutic effectiveness and thus improve the lives of patients and their families in a timelier manner. Indeed, if you think you are overwhelmed by the current pace of your daily practice routine, just wait until tomorrow, hold on and see how you feel.

So, practically speaking, what will we be doing differently in the future? How will we spend our days? Undoubtedly, our procedural interventions will be different. Certainly, we will adapt to new therapies for familiar vascular and non-vascular conditions where the treatments we currently offer are limited in terms of effectiveness, accuracy, patient risk, speed, cost, comfort, durability, etc. Some of our current procedures will be effectively applied to diseases and lesions not encountered in our present practice (obesity, neurodegenerative diseases, diabetes, mental illness, prostatic hypertrophy, selected orthopedic conditions, etc.).

Old guidance systems, usually not considered an integral part of the IR armamentarium, such as direct visualization using fiber optic scopes, will be re-configured with creative designs to enable us to enter new fields of therapy (sinus, bariatric, and ablative procedures) to deliver less-invasive solutions. In addition, completely new integrated guidance and intra-procedural monitoring systems based on image fusion, robotics and feedback from a variety of tissue bio-parameters tracked during therapy will create new value by incorporating "more effective" into the less-invasive promise of safer, faster, and better tolerated. Finally, completely unanticipated, unimagined and novel new procedures will be introduced and validated as alternatives for patients who now have only medical or open surgical options.

It is without fail a safe bet that less invasive interventional opportunities will continue to grow with technological advances that clearly promise to impact clinical practice and transform medicine. Economic and political forces will have key roles in creating these changes. IR needs to assume a leadership position in contributing to the future evolutionary process. We all need to prepare for these inevitable developments.

Jan Peregrin
CIRSE President

Portrait of the new CIRSE President

Jan Peregrin was born in Hradec Králové in Czechoslovakia (now Czech Republic). In 1975 he graduated from Charles University medical school located in the same city. After graduation he joined the Department of Radiology at the Institute for Clinical and Experimental Medicine in Prague. "My good fortune was that the head of this department was one of the pioneers of Interventional Radiology in Europe, Alfred Belán and I had the opportunity to carry out IR procedures from their very beginning." says Peregrin of his time at the department. J. Peregrin has since worked at this department, except for the time between 1984 and 87, when he worked at the University of Kuwait. Upon the retirement of Professor Belán J. Peregrin replaced him as the chairman of the department in 1991.

As the orientation of the department originally was mainly cardiovascular and following the practice of the day, J. Peregrin started his career performing mainly peripheral and coronary angiography, later followed by peripheral and coronary angioplasty. When cardiologists started carrying out cardiac interventions, J. Peregrin stayed with the peripheral arterial and venous interventions, later branching out to nonvascular procedures (biliary drainage and nephrostomy).

The profile of Prof. Peregrin's Institute – a facility loosely affiliated with the Charles University – has slowly evolved, focusing on three main specialties: cardiovascular procedures, transplantations (approx. 200 kidneys and over 60 livers per year) and diabetology (mainly diabetic foot). As the department also had to serve the purpose of the Institute, it was never short of diagnosing as well as vascular and nonvascular complications of kidney and liver transplantations. As mentioned earlier, another important focus has been the endovascular treatment of ischemic complications of the diabetic foot as well as the treatment of other peripheral vascular diseases.

Prof. Peregrin's special interests lie in renal artery PTA (particularly in children and patients with kidney transplants), transplanted kidney nephrostomy and other nephrostomy related interventions, biliary interventions in transplanted livers and infrapopliteal interventions in patients with critical lower limb ischemia.

Together with colleagues from other departments he is currently working on two main research pro-jects: percutaneous transplantation of islet cells in patients with diabetes and the development and animal testing of a mechanical percutaneous aortic valve.
In his spare time J. Peregrin's enjoys skiing, tennis and table tennis, listening to music from the sixties and reading science fiction and fantasy novels.

Prof. Peregrin joined CIRSE in 1985. Since then he has participated in all CIRSE congresses. He has been a member of the Executive Committee since 1998, first joining as the Local Host Committee Chairman of the Prague meeting. Later on he served in various positions, including as Programme Planning Committee Chairman for the congresses in Lucerne and Belek and as treasurer from 2005 until 2007. Having been elected as Vice President in 2007, he will replace Jim Reekers in the position of President this September.

"Becoming President of CIRSE is both, easy and difficult for me." says Peregrin. "It can be seen as easy, as I am taking over a very sound and rapidly growing society with healthy finances and an expanding educational programme. But it can also be seen as difficult, because it will be a challenge to keep up with the high level set by my very successful predecessors – Andy Adam, Johannes Lammer and Jim Reekers."
Nevertheless I am confident that I will be able to start many new projects and continue CIRSE's success story.

Shape the future

The European School of Interventional Radiology (ESIR) is an initiative by the CIRSE Foundation to create a worldwide platform for interventional radiologists to further their skills, increase their knowledge and broaden their action margin within Interventional Radiology.

ESIR is based on the cooperation of interventionists from across Europe and overseas, including key opinion leaders in numerous countries and national IR societies.

ESIR offers a multitude of educational tools !

The Courses

ESIR offers intense two-day courses and workshops on specific procedures in numerous European countries, limited participant numbers offering best possible student-tutor interaction.
ESIR's Spring Meetings focus on a specific field of Interventional Radiology, offering sessions, workshops and symposia on embolization and Interventional Oncology.

The Grants

Every year ESIR awards Fellowship and Visiting Scholarship grants with a total value of € 100,000 to young interventional radiologists wanting to further their skills in another centre of excellence.

The Web

With the aim of providing IR education around the year and to all parts of the world, ESIR has created an educational online database. www.esir.org allows all CIRSE members to view and download 2,800 titles including videos, abstracts, EPOS presentations and slide shows from previous CIRSE meetings free of charge.

ESIR

European School of Interventional Radiology

2010 Highlights

ECIO 2010

European Conference on Interventional Oncology

April 21-24
Florence | Italy
www.ecio2010.org

ICCIR 2010

International Conference on Complications in Interventional Radiology

June 10-12
Poertschach | Austria
www.iccir2010.org

CIRSE foundation | www.cirse.org

Techniques and results on subclavian stenosis/occlusion

Don't miss it !
Controversies in vascular intervention
Special Session
Tuesday, September 22,10:00-11:00
Auditorium 1

Elias N. Brountzos
Associate Professor of Intervetional Radiology
2nd Department of Radiology
Attikon University Hospital
Athens, Greece

The innominate artery, the common carotid and the subclavian artery are collectively named aortic arch arteries or brachiocephalic arteries. Symptomatic lesions of these arteries occur less frequently than symptomatic lesions of the carotid bifurcations. The joint study of arterial occlusion reported that only 17% of lesions demonstrated on arteriography involved the innominate artery and the proximal subclavian arteries (1).

Innominate artery and subclavian artery occlusive disease occurs in relatively younger patients than more common types of atherosclerotic disease. Mean age ranges from 49 to 69 years. There is only a slight predominance of male patients in most of the reports. In some of the reports female patients represent the majority (2).

Comorbid conditions
Concomitant coronary artery disease is present in about 50% of patients with innominate or subclavian artery occlusive lesions, peripheral artery disease is present in 27% of patients, and carotid and vertebral artery lesions are present in 29% of patients (3). These numbers reflect the disease extent and severity, with two thirds of the patient population having multiple supra-aortic and coronary lesions. Because of the serious comorbid conditions these patients have high surgical risk, which is responsible for the increased morbidity and mortality rates associated with surgical reconstructions.

History
A patient with symptoms of subclavian artery occlusion was first reported by Savory in 1856 (4). In 1944 Martonell and Fabre reported of a patient with occlusive disease of all great vessels, the so-called "Martonell syndrome" (5). In 1956 Davis et al performed the first trans-thoracic innominate artery endarterectomy (6) and prosthetic bypass grafting was introduced by DeBakey et al. in 1958 (7). These operations were associated with a considerably high operative mortality rate. Due to these concerns extra-anatomic procedures were developed to reduce the operative risk. Diethrich et al. analysed the Houston group's experience with 125 cases of carotid-subclavian artery bypass grafts in 1967, thus popularising this operation (8). The mortality rate was reduced from 22% with transthoracic repair to 5.6% with carotid-subclavian bypass grafting.

Percutaneous transluminal angioplasty (PTA) of the aortic arch branches was introduced in 1980 by Mathias et al. and Bachman and Kim, and has subsequently evolved as an effective and safe treatment modality for occlusive lesions of the subclavian and innominate arteries (9,10).

The indications for treatment of the aortic arch vessel occlusive disease are controversial. The presence of abundant collateral circulation makes the clinical significance of a particular lesion difficult to predict. As a general rule only symptomatic patients should be treated. An additional indication is the preservation of the inflow for a planned surgical bypass, like axillo-femoral or left internal mammary, to coronary artery grafts (LIMA).

Lesions of the subclavian arteries are more common than lesions of other aortic arch branches. The left subclavian artery is more often involved than the right. Patients with isolated subclavian artery lesions are often asymptomatic because of the presence of rich collateral supply. When symptomatic, the patients present with upper limb ischemia, ischemia of the posterior cerebral circulation or both (11).

The radiographic subclavian artery steal alone as depicted by DSA or Duplex sonography has been disputed as a cause of neurological symptoms, especially in the absence of concomitant extracranial occlusive lesions. It is rather considered a normal pattern of collateral response to proximal subclavian artery occlusion (12). However, proximal lesions of the subclavian artery may be symptomatic. Those patients suffer from symptoms of vertebrobasilar insufficiency, such as visual disturbances, often bilateral, vertigo, ataxia, syncope, dysphasia, dysarthria, sensory deficits of the face and motor and sensory deficits of the extremities. Symptoms of the upper extremities include muscle fatigue, "arm claudication", rest pain and digital necrosis from atheroembolization.

Physical examination is invaluable for the diagnosis. Cervical bruits, absent brachial artery pulses or blood pressure difference in the arms are suggestive of occlusive disease of the subclavian arteries. Finger ulcers or skin changes may indicate atheroembolization from ulcerated lesions. Imaging diagnosis can be achieved by Colour Doppler ultrasonography, but CTA and MRA or DSA are more reliable.

Surgical Treatment
Surgical options include carotid-subclavian bypass using synthetic grafts or saphenous vein and transposition of the subclavian artery up to the common carotid artery. Both techniques have low mortality and stroke rates of 0-1.4% and 0.5%-5% respectively. Patency rates are very good with 5-year and 10-year patency of 92-95% and 83-95% respectively (13).

Endovascular treatment
Endovascular methods are attractive therapeutic alternatives due to their minimal invasiveness and better patient tolerance. The interventional therapy is indicated only in symptomatic patients. Additional indication includes increasing the inflow for scheduled operative procedure, i.e. LIMA graft, axillo-femoral graft or dialysis graft. The procedure is contraindicated whenever there is thrombus adjacent to the lesion, as it increases the risk of brain embolization.

Technique
In our practice the procedure is performed with local anaesthesia under conscious sedation. Although some operators have used general anaesthesia, most operators prefer local anaesthesia.

The most preferred access artery for the treatment of stenotic lesions is the femoral artery, although the brachial or the axillary artery have been routinely used by some operators. The brachial approach is associated with increased access artery thrombosis rates due to the small vessel caliber. With the introduction of modern low profile balloons and stent systems this problem may be obviated. The advantage of the brachial artery approach lies in the shorter and less tortuous path to the lesion; this is important in the case of total occlusions which are often impossible to cross from the groin, thus necessitating the brachial approach.

Primary stent placement is practiced in the most recent series. However, there is no study proving the benefit of using stents as a primary treatment. Balloon expandable stents are more frequently used, but self- expanding stents are used especially in long (>40 mm) lesions. It is accepted that stenting across the origin of the vertebral artery should not be done. Uncomplicated patients are discharged on antiplatelet regimen only, although patients with vascular comorbidities are prescribed clopidogrel.

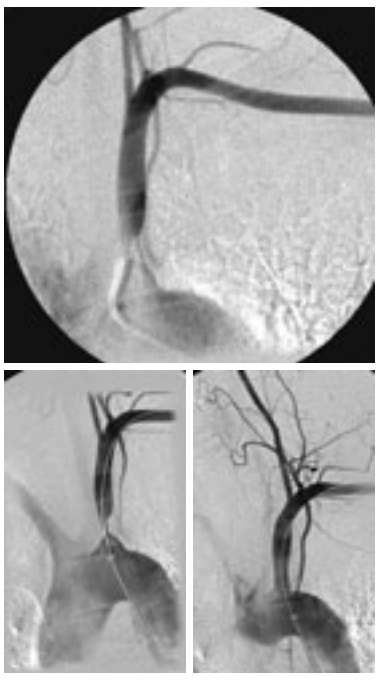
Results
The technical success is excellent: 90-100% for stenoses, 25-95% for occlusions. The procedures can be accomplished without perioperative mortality, while the stroke rate is 0.9-1.4% - significantly better than open surgery, which justifies the enthusiastic use of these methods.

In our experience as well as in the literature short-term patency rates are excellent: 2-year patency of 91-92% has been reported (11). Long-term patency rates are inferior to surgery, although no randomised studies have been published. In a recent comparison between stent treatment and carotid-subclavian bypass using synthetic conduits (CSBG) the primary patency rates at 1, 3, and 5 years were 100%, 98%, and 96% for the CSBG group versus 93%, 78%, and 70% for the stent group, respectively ($p<0.0001$). Freedom from symptom recurrence was also statistically superior in the bypass group versus the stent group ($p<0.0001$). There was no difference in the survival rates between the two groups (14).

In summary, the interventional treatment of subclavian artery stenoses and occlusions is advocated only in symptomatic patients. Although long-term patency rates are inferior to surgery, the interventional treatment is the first choice, as it has minimal mortality and morbidity.

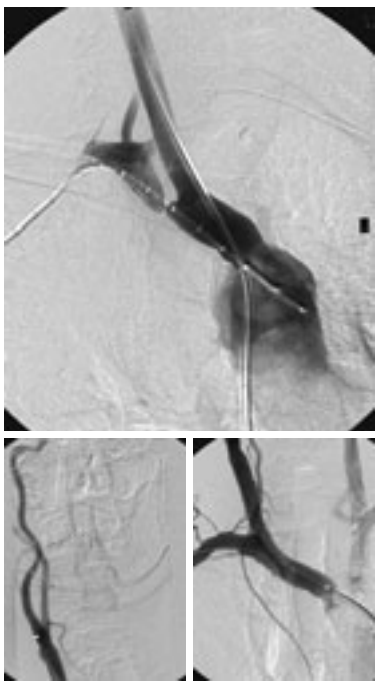
References:
1. Fields WS, Lemak NA. Joint study of extra-cranial arterial occlusion. Subclavian steal: a review of 168 cases. JAMA 1972; 222:1139-1143.
2. Schillinger M, Haumer M, Schillinger S, Ahmadi R, Minar E. Risk stratification for subclavian artery angioplasty: is there an increased rate of restenosis after stent implantation? J Endovasc Ther 2001; 8:550-7.
3. Kieffer E, Sabatier J, Koskas, et al. Atherosclerotic innominate artery occlusive disease: early and long-term results of surgical reconstructions. J Vasc Surg 1995; 2: 326-337.
4. Savory WS. A case of a young woman in whom the main arteries of the both upper extremities, and of the left side of the neck, were throughout completely obliterated. Med Chir Trans 1856; 39: 205
5. Martonell F, Fabre J. El syndrome de obliteracion de los troncos supraaorticos. Med Clin 1944 ;2 :26-30.
6. Davis JB, Grove WJ, Julian OC. Thrombic occlusion of branches of aortic arch. Martonell's syndrome: Report of case treated surgically. Ann Surg 1956;144:124-126.
7. DeBakey ME, Morris GC, Jordan GL, et al. Segmental thromboobliterative disease of the great vessels arising from the aortic arch. JAMA 1958; 166: 998-1003.
8. Dietrich EB, Garrett HE, Ameriso J, et al. Occlusive disease of the common carotid and subclavian arteries treated by carotid-subclavian bypass. Am J Surg 1967; 114:800-8.
9. Mathias K, Schlosser V, Reinke M (1980). Katheterrekanalisation eines Subklaviaverschlusses. RoFo 132: 346-347.
10. Bachman DM, Kim RM (1980). Transluminal dilatation for subclavian steal syndrome. Am J Roentgenol; 135: 995-6.
11. Brountzos EN, Petersen B, Binkert C, Panagiotou I, Kaufman JA. Primary stenting of subclavian and Innominate artery occlusive disease: A Single Center Experience. Cardiovasc Intervent Radiol 2004; 27: 616-623.
12. Parrott JC. The subclavian steal syndrome. Arch Surg 1964; 88: 661-665.
13. Vitti MJ, Thompson BW, Read RC, et al. Carotid-subclavian bypass: A twenty-two-year experience. J Vasc Surg 1994; 20:411-418.
14. AbuRahma AF, Bates MC, Stone PA, et al. Angioplasty and stenting versus carotid-subclavian bypass for the treatment of isolated subclavian artery disease. J Endovasc Ther. 2007 ;14:698-704.

Fig.1: A 45-year old female patient presented with leg arm claudication caused by a left subclavian artery stenosis which was treated with angioplasty with stent placement.



a: Selective left subclavian artery DSA depicts a tight stenosis within one cm of the ostium.
b: DSA performed through a 6-F 90 cm in length sheath following the crossing of the stenosis with a guidewire.
c: Completion DSA following angioplasty with a 10X 30 mm self expandable stent dilated with a 10X 30 mm balloon depicts technical success.

Fig.2: A 70-year old patient with right arm claudication caused by a stenotic lesion of the right subclavian artery. Angioplasty with stent using right internal carotid artery embolic protection.



a: right innominate artery DSA performed with a calibrated pigtail catheter placed via the right brachial artery depicts a tight stenosis at the ostium of the right subclavian artery. Note a 5-F 90 cm sheath placed via the right common femoral artery in the right common carotid artery.
b: Right common carotid DSA depicts the embolic protection device in the right internal carotid.
c: Completion DSA following angioplasty with a 10X30-mm balloon explandable stent depicts technical success.

Cordis®
a Johnson & Johnson company

Ground breaking, Life changing™

Endovascular

Get back into the **true lumen** with ease and precision

OUTBACK® LTD™ Re-Entry Catheter

True Lumen Re-Entry Technology

- Precise and predictable orientation and deployment to ensure optimal patient outcomes
- No need for additional visualization equipment
- Easy, rapid manoeuvring with one-to-one torque response
- Helps reduce time under fluoroscopy and may help increase procedure throughput

2E-840-0117-1 • Tel: +32 2 352 14 11 • Fax: +32 2 352 15 90

50 Year Anniversary

Cordis
PRODUCTS SERVICES OUTCOMES

Imaging and diagnosis of chronic venous insufficiency

António Miguel Madureira
Vascular and Interventional Radiology Unit
Hospital São João
Porto, Portugal

Don't miss it !
Venous disease
Special Session
Wednesday, September 23, 08:30-09:30
Auditorium 6

The peripheral venous system functions both as a reservoir and as a conduit to return blood from the legs to the heart, uphill, against gravity and against fluctuating thoracoabdominal pressures. Its correct functioning depends on a series of unidirectional valves, present on the superficial, the deep and the perforator veins that direct blood proximally and deeply driven by the motive force of the musculovenous pump (the calf muscle pump).
The superficial venous system is a web-like network of interconnecting, multilayered veins which collects blood from the dermis and hypodermis and sends it to the deep system through the perforators.
The great saphenous vein (GSV) originates in the medial dorsal venous arch of the foot, passes anterior to the medial malleolus to the medial aspect of the leg, then behind the medial femoral condyle and continues in the anteromedial thigh in a fascial envelope superficial to the muscular fascia, the saphenous compartment (Fig.1). It joins the common femoral vein at the groin crease, the saphenofemoral junction (SFJ).
Most patients have two major tributaries below the knee, the anterior and posterior, and two above the knee, the anterior circumflex and posterior circumflex. There are three pelvic veins that commonly drain at the SFJ, the superficial external pudendal, the superficial inferior epigastric and the superficial circumflex iliac. There may be anterior or posterior accessory GSVs, which parallel the main trunk superficially, and duplicated GSVs, which run in the saphenous compartment. The GSV is closely associated with the saphenous nerve in the lower leg.
The small saphenous vein (SSV) originates in the lateral dorsal venous arch of the foot, passes posterior to the lateral malleolus and ascends in the midline in a saphenous compartment. It may penetrate the deep fascia at any point from the middle third of the calf upward and may drain to the popliteal vein (the saphenopopliteal junction – SPJ) and/or to deep veins at higher level via a thigh extension deep to the muscular fascia and/or to the proximal GSV via the Giacomini vein (the thigh extension and the posterior circumflex tributary). The SSV is intimately associated with the sural nerve in the distal calf.
The perforator veins pierce the deep muscular fascia and join the superficial and deep veins. The old nomenclature has been replaced by a topographic nomenclature.

The deep venous system collects the blood from the musculoskeletal structures and receives the blood from the superficial system. In the lower leg there are three pairs of deep veins: the anterior tibial, the posterior tibial and the peroneal. Just below the knee these join to form the popliteal vein, which is called femoral vein (formerly superficial femoral vein) proximal to the adductor canal. The popliteal vein also drains the soleal and gastrocnemius intramuscular venous plexi. The deep femoral vein originates from terminal muscle tributaries of the lateral thigh, joins the femoral vein in the proximal thigh and forms the common femoral vein, which becomes the external iliac vein above the groin crease.
The muscles of the calf and foot function as a "peripheral heart" squeezing the deep veins in their fascial muscle compartment. Muscle contraction opens up the outflow valve of the deep vein segment above at the same time as it closes the intake valves from the perforators and from the deep vein segment below.
The most frequent form of chronic venous insufficiency (CVI) is primary insufficiency of the superficial system, caused by congenitally insufficient valves or by congenitally weak walls. Secondary causes include muscle pump failure, outflow obstruction and secondary incompetence. The impairment in venous return results in failure to lower pressure in the distal veins of the leg while walking (ambulatory venous hypertension) and reduces the arterial inflow. The increased hydrostatic pressure and dilatation lead to sequential valve failure downwards, like a domino.
Patients should be evaluated regarding the clinical findings (C), the aetiology of the insufficiency (E), its anatomical distribution (A) and the pathologic mechanism of development (P), according to the revised CEAP classification (Table 1).
A thorough medical history and physical examination guides the choice of additional diagnostic studies. A positive family history, previous thromboembolic events, female sex, parity, increasing age, immobility, tobacco abuse and standing occupations are known risk factors. The patient should be inspected from foot to umbilicus, looking for telangiectasias or spider veins and reticular and varicose veins. Skin changes are seen at the distal portion of the vein, so the medial ankle region (GSV) and the lateral ankle region (SSV) should be carefully inspected.
Duplex ultrasound is the key examination technique. The evaluation of the deep system is performed with the patient supine and that of the superficial system standing, preferably on a platform, with the non-weight-bearing extremity evaluated.

The GSV is usually less than 4 mm in diameter in the mid-thigh and the SSV less than 3 mm in the upper calf, but there can be significant truncal reflux without dilatation, possibly because, unlike their tributaries, they run in a taut fascial compartment (Fig.2). A perforator vein 3.5 mm in diameter has a 90 % chance of having significant reflux (Fig.3).
The most reliable sign of thrombosis is inability to collapse the lumen by exerting pressure with the transducer (Fig.4); in B–mode this diagnosis is also suggested by a hyperechoic lumen and altered diameter. In colour Doppler-mode patency and flow hemodynamic are checked and characterised by spectral Doppler sampling. Veins should have respiratory variations (Fig.5) and the normal valve function should result in retrograde flow not greater than 0.5 seconds in all veins excluding the common femoral vein (not greater than 1.5 seconds) (Fig.6). Distal manual compression seems to be the most reliable manoeuvre to test for reflux. The highest frequency transducer and the most sensitive Doppler settings available should be chosen in order to be able to diagnose slow-moving blood.
Photoplethysmography relies on the absorption of infrared light by haemoglobin to document venous congestion on the distal leg, providing functional information. In patients with deep and superficial reflux it is able to quantify the relative contribution of each system, and in the setting of DVT it may help to define the role superficial varicose veins play in the venous outflow. In patients presenting with unusual forms of leg pain it may contribute to rule out venous aetiology.
Conventional venography is now seldomly used. In ascending venography, iodinated contrast injected into a superficial vein is followed as it ascends through the extremity; tourniquets can be used to compartmentalise the superficial veins and to allow identification of retrograde flow through incompetent perforating veins. A conventional femoral vein puncture enables the evaluation of the iliac and uppermost femoral veins to advantage, being also necessary in descending venography which evaluates venous valve incompetence.
Computed Tomography (CT) and Magnetic Resonance (MR) are helpful in situations of uncertainty or of ambiguity. They provide information on the lumen, the wall, and the surrounding tissues, distinguishing acute from chronic signs and can consistently depict the deep veins of the lower extremity and the pelvic and abdominal sources of varicosities.
CT has been extensively used for the diagnosis of venopulmonary thromboembolic disease. Multidetector CT has sufficient spatial resolution to show superficial veins 2 mm in diameter. Non-contrast enhanced three-dimensional (3D) CT adequately visualises the superficial veins in the hypodermis fat, but not the perforator or deep veins. Indirect contrast-enhanced 3D CT venography, through an antecubital vein injection, can show all the perforator veins of the lower extremity, yielding a road map of the superficial and perforator veins.
MR venographic techniques have refined; 3D contrast-enhanced venography of the deep system is now possible through an antecubital vein injection, and unenhanced flow-independent MR venograpy seems promising for the study of both, the deep and the superficial venous systems. MRV does not use ionising radiation and the gadolinium-based contrast has a better nephrographic profile.

References:
1. Abu-Hijleh M F, Roshier A L, Al-Shboul Q, Dharap A S, Harris P F. The membranous layer of the superficial fascia: evidence for its widespread distribution in the body. Surg Radiol Anat 2006; 28:606-619
2. Bahcivan M, Elmali M, Karamustafa H, Aslan S, Diren H B. A Rare Cause of Pulmonary Emboli in a Patient with Deep Vein Thrombosis: Doppler Ultrasonographic Compressibility Maneuver. Cardiovasc Intervent Radiol 2007; 30:803-805
3. Caggiati A. Fascial relations and structure of the tributaries of the saphenous veins. Surg Radiol Anat 2000; 22:191-196
4. Caggiati A. The saphenous venous compartments. Surg Radiol Anat 1999; 21:29-34
5. Cham M D, Yankelevitz D F, Shaham D, Shah A A, Serman L, Lewis A, Rademaker J, Pearson G, Choi J, Wolff W, Prabhu P M, Galanski M, Clark R A, Sostman H D, Henschke C I. Deep Venous Thrombosis: Detection by Using Indirect CT Venography. Radiology 2000; 216:744-751
6. Doyle J F. Fascial relations and connections of the short saphenous vein. Ir J Med Sc 1967; 317-323
7. Edelman R R, Koktzoglou I. Unenhanced Flow-Independent MR Venograpy by Using Signal Targeting Alternative Radiofrequency and Flow-Independent Relaxation Enhancement. Radiology 2009; 250:236-245
8. Fegan W G, Fitzgerald D E. A Clinical Classification of the Anatomy of the Perforating Veins of the Leg. Ir J Med Sc 1963; 439-443
9. Fraser D G W, Moody A R, Davidson I R, Martel A L, Morgan P S. Deep Venous Thrombosis: Diagnosis by Using Venous Enhanced Subtracted Peak Arterial MR Venography versus Conventional Venography. Radiology 2003; 226: 812-820
10. Fronek, H S. The Fundamentals of Phlebology: Venous Disease for Clinicians. 2nd Edition. American College of Phlebology 2008
11. Ghaye B, Szapiro D, Willems V, Dondelinger R F. Pitfalls in CT Venography of Lower Limbs and Abdominal Veins. AJR 2002; 178:1465-1471
12. Holtz D J, Debatin J F, McKinnon G C, Unterweger M, Wildermuth S, Schulthess G K, Fuchs W A. MR Venography of the Calf: Value of Flow-enhanced Time-of-Flight Echoplanar Imaging. AJR 1996; 166:663-668
13. Lee W, Chung J W, Yin Y H, Jae H J, Kim S J, HA J, Park J H. Three-Dimensional CT Venography of Varicose Veins of the Lower Extremity: Image Quality and Comparison With Doppler Sonography. AJR 2008; 191:1186-1191
14. Lebowitz J A, Rofsky N M, Krinsky G A, Weinreb J C. Gadolinium-Enhanced Body MR Venography with Subtraction Technique. AJR 1997; 169:755-758
15. Min R J, Khilnani N M, Golia K. Duplex Ultrasound Evaluation of Lower Extremity Venous Insufficiency. JVIR 2003; 14:1233-1241
16. Moore, Dalley. Clinically Oriented Anatomy. 5th Edition. LWW 2005
17. Prince M R, Sostman H D. MR Venography: Unsung and Underutilized. Radiology 2003; 226:630-632
18. Ruehm S G, Wiesner W. Pelvic and Lower Extremity Veins: Contrast-enhanced Three-dimensional MR Venography with a Dedicated Vascular Coil – Initial Experience. Radiology 2000; 215:421-427
19. Rutherford R B, Vascular Surgery. 6th Edition. Saunders 2005

Table 1: The CEAP Classification

CLASSIFICATION		SYMPTOM
Clinical	C_0	No visible or palpable signs of venous disease
	C_1	Telangiectasias or reticular veins
	C_2	Varicose veins
	C_3	Edema
	C_{4a}	Pigmentation or eczema
	C_{4b}	Lipodermatosclerosis or atrophic blanche
	C_5	Healed venous ulcer
	C_6	Active venous ulcer
	A	Asymptomatic
	S	Symptomatic[1]
Etiologic	E_c	Congenital
	E_p	Primary
	E_s	Secondary (usually postthrombotic)
	E_n	No venous cause identified
Anatomic	A_s	Superficial veins[2]
	A_d	Deep veins[3]
	A_p	Perforator veins[4]
	A_n	No venous location identified
Pathophysiologic	P_r	Reflux
	P_o	Obstruction
	$P_{r,o}$	Reflux and obstruction
	P_n	No venous pathophysiology identified

1 Clinical severity score and disability score are useful adjuncts
2 Subdivided in (1) Telangiectasias or reticular veins, (2) GSV above the knee, (3) GSV below the knee, (4) SSV, (5) Non saphenous
3 Subdivided in (6) IVC, (7) Common iliac, (8) Internal iliac, (9) External iliac, (10) Pelvic, (11) Common femoral, (12) Deep femoral, (13) Femoral, (14) Popliteal, (15) Sural, (16) Muscular
4 Subidvided in (17) Thigh, (18) Calf

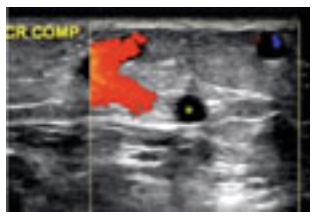


Fig.1: The truncal GSV (*) in its fascial compartment. Tributary veins are seen outside (right) and piercing the membranous layer of the saphenous envelope (left).

Fig.4: A. Left popliteal vein (*) collapse with pressure exerted on the transducer (right). Its lumen shows no echoes. B. Common femoral vein (*) and GSV (**) are not collapsable and exhibit endoluminal hyperechogenicity (signs of thrombosis).

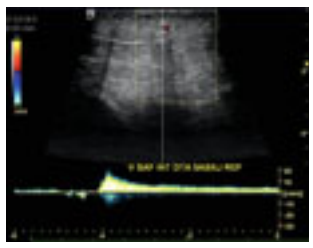


Fig.2: Triplex imaging: B-mode, colour-doppler mode and spectral-doppler mode of the GSV: insufficient. Reflux longer than two seconds with no dilatation. The transducer is in the transverse plane, angled towards the head of the patient.

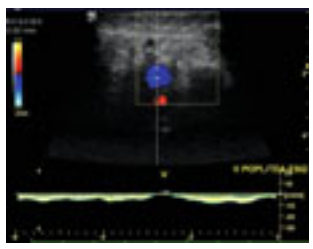


Fig.5: Left popliteal vein: normal. Gentle respiratory variations and short reflux with Valsalva manoeuvre. The transducer is in the trasverse plane, angled towards the head of the patient.

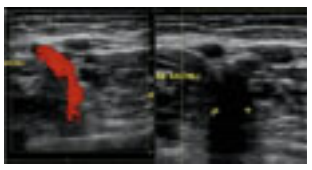


Fig.3: Perforator vein in the distal medial thigh: insufficient. Colour-doppler image (left) shows reflux (forward flow towards the superficial venous system) and B-mode image shows dilatation (diameter of 4 mm).

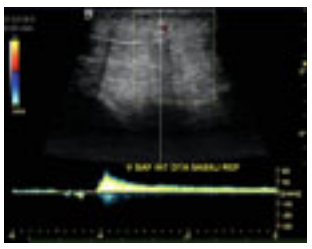
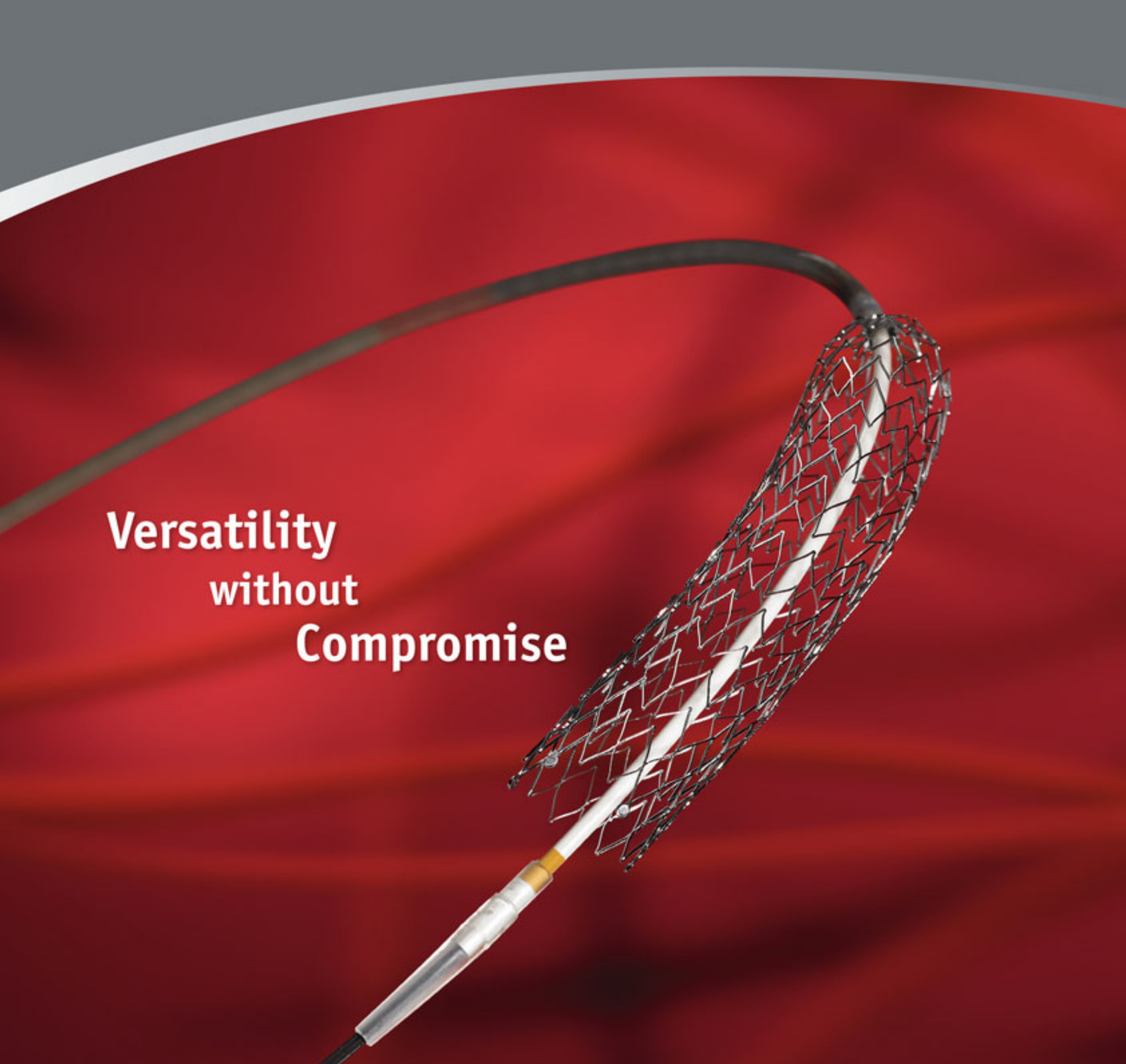


Fig.6: Right popliteal vein: insufficient. With manual distal compression a forward, upward, flow (graphic below the horizontal, basal, line) is followed by a retrograde, downward, flow (graphic above the basal line). The transducer is in the trasverse plane, angled towards the head of the patient.



Epic™ Self-Expanding Nitinol Vascular Stent with Delivery System

Designed for optimal balance between radial force, flexibility and durability, the Epic™ Self-Expanding Nitinol Vascular Stent with Delivery System is built to deliver accurately and easily. Available stent diameters from 5-14 mm and stent lengths from 20-120 mm. 6F (2.00 mm OD) sheath compatibility across all stent sizes, with room to inject contrast.

www.bostonscientific-international.com

Boston Scientific

Delivering what's next.™

Jeff F. Geschwind
Professor of Radiology, Surgery and Oncology
Director, Interventional Radiology Center
Johns Hopkins University School of Medicine
Baltimore, USA

Future of Catheter Guided Cancer Therapy

The role of catheter-based image-guided therapy in the management of patients with cancer has grown tremendously in the last decade. It is likely to become even more important in the era of personalised medicine and as a result of the advent of agents able to target specific sites within cancer cells.

a. Antiangiogenic therapy in combination with chemoembolization for liver cancer

Emerging data have demonstrated the importance of angiogenesis in the pathogenesis of hepatocellular carcinoma (HCC). Indeed, excessive and abnormal vasculature (microvessel density) and increased levels of vascular endothelial growth factor (VEGF) are now considered hallmarks of HCC (1). High VEGF expression has also been associated with lower patient survival (1). Interestingly, and in contrast to the traditional belief that tumour ischemia is favourable, several studies have shown that tumour hypoxia 1) up-regulates several pathways, including pro-angiogenic factors that are clearly detrimental to tumour control, 2) provides resistance to apoptosis, 3) stimulates the growth of cancer cells, 4) up-regulates tumour metabolism, and finally, 5) promotes tumour invasion (2,3). Antiangiogenic therapy therefore represents an attractive approach against HCC.

Bevacizumab (Avastin™, Genentech Inc., San Francisco, CA), a humanised monoclonal antibody that binds vascular endothelial growth factor (VEGF) and prevents its interaction to receptors on the surface of endothelial cells, has recently emerged as an important therapeutic agent in various cancers. In addition to its direct antiangiogenic effects, bevacizumab may enhance chemotherapy administration by normalising tumour vasculature and decreasing the elevated interstitial pressure in tumours. A recent pilot study suggested that bevacizumab can be given safely at both 5 and 10 mg/kg in HCC patients with localised unresectable HCC, preserved liver function and no significant esophageal varices (4).

In a pilot study selected HCC patients undergoing transcatheter arterial chemoembolization (TACE) additionally received intravenous bevacizumab which was well tolerated and prolonged disease control (5). Currently there are two NCI-endorsed phase II trials evaluating the safety and efficacy of bevacizumab in patients with primary unresectable liver cancer. Our phase II trial of bevacizumab administered IV (10mg/kg) 1 week before TACE and then again at the time of TACE and 2 weeks after, for patients with HCC has completed enrollment (30 patients). Preliminary results showed excellent toxicity profile and a favourable tumour response by imaging. Survival data are promising with PFS around 18 months.

Sorafenib, the orally available multitargeted receptor tyrosine kinase inhibitor (Nexavar; Bayer, west Haven, CT and Onyx, Emeryville, CA) is the first agent to demonstrate survival benefit in two separate randomised trials and has been approved by the US FDA. A phase II safety study combining sorafenib with doxorubicin-eluting microspheres (DC Bead™; Biocompatibles, Surrey, UK) for patients with HCC was just started in our institution. This will be followed by a worldwide randomised trial. Data from these trials may guide to the development of novel antiangiogenic liver cancer regimens. It is important to note that successful execution of these trials depends not only on the transfer of expertise from the bench to the bedside, but also on the productive collaboration of clinicians in a multidisciplinary oncologic setting.

b. Drug-eluting beads chemoembolization for liver cancer

The issue of drug delivery to tumours is critically important in oncology. Ideally, drug-loaded carriers should be able to deliver drugs in a precise, controlled and sustained manner in order to achieve high intra-tumour drug concentration for a sufficient period without damaging the surrounding hepatic parenchyma. Several drug-delivery systems for intra-arterial treatment of hepatic lesions, such as polyvinyl alcohol microspheres and plcg-microspheres, have been tested recently (6-8). Polyvinyl alcohol (PVA) hydrogel microspheres can be loaded with a single chemotherapeutic agent, such as doxorubicin or irinotecan and infused intrarterially for selective tumour targeting (9).

Doxorubicin-eluting beads (DEB) were initially tested on the rabbit Vx-2 tumour model and demonstrated consistent drug release over time with excellent tumour control and lower serum levels of drug. Based on these results a number of clinical trials were launched worldwide. Pharmacokinetic data obtained from some of these clinical trials revealed significantly lower serum levels treated with DEB-chemoembolization than those treated with classic chemoembolization (10).

Objective response rates by imaging (EASL criteria: European Association for the Study of the Liver; based on lack of contrast enhancement) ranged from 60 to 90 % (11, 12), with some patients showing complete response by EASL (Fig. 1a, b, c). Survival rates also appear improved over those obtained with conventional TACE (93% at 6 months to 89% at 2 years) (11, 12). In summary, TACE using DEB has so far shown promising results both in terms of tumour response and patient survival and is likely to replace conventional TACE if the data from clinical trials remain positive.

c. Targeting tumour metabolism: A new approach to liver cancer

Tumours depend on energy production pathways that are different from those of normal cells. In fact, whereas normal cells rely on oxidative phosphorylation, tumour cells rely almost exclusively on glucose metabolism for their energy needs, required for their growth. This phenomenon has been used as a diagnostic tool with positron emission tomography (FDG PET), but never exploited as a therapeutic target. 3-Bromopyruvate (3-BrPA), a specific alkylating agent and potent ATP inhibitor, has been shown (in vitro) to disrupt this metabolic pathway, thereby leading to the demise of the cancer cells through apoptosis (13, 14). This potent agent has already been tested via transcatheter infusion in various animal models of cancer (15).

In studies conducted in the rabbit Vx-2 liver tumour model, direct intra-arterial infusion of 3-BrPA showed complete tumour destruction, without affecting the surrounding normal liver parenchyma (15) (Fig. 2a, b, c, d). In more recent studies, the effective therapeutic dose of 3-BrPa was established, leading to complete cures of the animals previously implanted with the Vx-2 tumour. In addition, FDG-PET imaging has proven quite useful to determine adequate delivery of the drug to the target tumour, assess tumour response after therapy with 3-BrPa and detect possible tumour recurrence (Fig. 3a, b). 3-BrPa is now being tested in human cancer cell lines transplanted in animals (xenografts). The results have so far matched those demonstrated in the Vx-2 rabbit model.

This entirely new anticancer approach is extremely promising and perfectly suited for catheter-based delivery. Clinical trials should be under way within one year.

Conclusion

Catheter based anticancer therapies have become readily accepted in the last decade and their impact on cancer patients will continue to grow. With the advent of newer targeted agents that can be given intra-arterially or systemically, the potency of transcatheter therapies can be drastically increased. A number of clinical trials (Phase I/II/III studies) exploiting the synergy between these two anticancer therapeutic approaches are already under way. Preliminary results from these trials have already shown great promise. Further advances in the development of specific cancer therapeutics and drug delivery systems should provide a leap into the search for a cure against cancer.

References:

1. Fin RS, Xhu AX. Targeting angiogenesis in Hepatocellular carcinoma: Focus on VEGF and Bevacizumab.Expert Rev.Antican Ther 2009;9(4):503-509
2. Xiong ZP, Yang SR, Liang ZY, Xiao EH, Yu XP, Zhou SK, et al. Association between vascular endothelial growth factor and metastasis after transcatheter arterial chemoembolization in patients with hepatocellular carcinoma. Hepatobiliary Pancreat Dis Int. 2004 Aug; 3(3):386-90.
3. Kobayashi N, Ishii M, Ueno Y, Kisara N, Chida N, Iwasaki T, et al. Co-expression of Bcl-2 protein and vascular endothelial growth factor in hepatocellular carcinomas treated by chemoembolization. Liver. 1999 Feb;19(1):25-31.
4. Siegel AB, Cohen EI, Ocean A, Lehrer D, Goldenberg A, Knox JJ, Chen H, Clark-Garvey S, Wienberg A, Mandeli J, Christos P, Mazumdar M, Popa E, Brown RS, Rafii S, Schwartz JD. Phase II trial evaluating the clinical and biological effects of Bevacizumab in unresectable hepatocellular carcinoma. Journal of clinical oncology 2008;26(18): 2992-98.
5. Britten C, Finn RS, Gomes AS, Amado R, Yonemoto L, Bentley G, Mass R, Bussutil RW, Slamon DJ. A pilot study of IV bevacizumab in hepatocellular carcinoma patients undergoing chemoembolization. 2005 ASCO Annual Meeting; 2005; Orlando, Florida; 2005.
6. Qian J, Truebenbach J, Graepler F, Pereira P, Huppert P, Eul T, et al. Application of poly-lactide-co-glycolide-microspheres in the transarterial chemoembolization in an animal model of hepatocellular carcinoma. World J Gastroenterol. 2003 Jan;9(1):94-8.
7. Constantin M, Fundueanu G, Bortolotti F, Cortesi R, Ascenzi P, Menegatti E. Preparation and characterisation of poly(vinyl alcohol)/cyclodextrin microspheres as matrix for inclusion and separation of drugs. Int J Pharm. 2004 Nov 5;285(1-2):87-96.
8. Vallee JN, Lo D, Guillevin R, Reb P, Adem C, Chiras J. In vitro study of the compatibility of tris-acryl gelatin microspheres with various chemotherapeutic agents. J Vasc Interv Radiol. 2003 May;14(5):621-8.
9. Lewis AL, Gonzalez MV, Lloyd AW, Hall B, Tang Y, Willis SL, et al. DC Bead: In Vitro Characterization of a Drug-delivery Device for Transarterial Chemoembolization. J Vasc Interv Radiol. 2006 February 1, 2006;17(2):335-42.
10. Varela M, Real MI, Burrel M, Forner, Sala M, Brunet M, Ayuso C, Castells L, Montana X, Llovet JM, Bruix J. Chemoembolization of Hepatocellular carcinoma with drug eluting beads: Efficacy and doxorubicin pharmacokinetics. J Hepatol 2007;46:747-487.
11. Kettenbach J, Stadler A, Katzler IV, Schernthaner R, Blum M, Lammer J, Rand T. Drug-loaded microspheres for the treatment of liver cancer: Review of current results. Cardiovasc Intervent Radiol 2008;31:468-476.
12. Malagari K, Chatzimicheal K, Alexopoulou E, Kelekis A, Hall B, Dourakis S, Delis S, Gouliamos A, Kelekis D. Transarterial chemoembolization of unresectable Hepatocellular carcinoma with drug eluting beads: Results of an open-label study of 62 patients. Cardiovasc Intervent Radiol 2008;31:269-280.
13. Gwak G-Y, Yoon J-H, Kim KM, Lee H-S, Chung JW, Gores GJ. Hypoxia stimulates proliferation of human hepatoma cells through the induction of hexokinase II expression. Journal of Hepatology. 2005;42(3):358
14. Pereira Da Silva A P, El-Bacha T, Kyaw N, Sousa Dos Santos R, Seixas Da-Silva W,.Almeida F C.L, T.Da Poian A and Antonio Galina. Inhibition of energy producing pathways of HepG2 cells by 3-bromopyruvate. Biochem J.2009;417,717-726.
15. Vali M KA, Liapi E, Kowalski J, Hong K, Khwaja A, Torbenson MS, Georgiades C, Geschwind JFG. Intraarterial therapy with a new potent inhibitor of tumour metabolism (3-bromopyruvate): identification of therapeutic dose and method of injection in an animal model of liver cancer. J Vasc Interv Radiol 2007; 18(1): 95-101.

Don't miss it !

Future Technology
Special Session
Wednesday, September 23, 08:30-09:30
Room 3.A

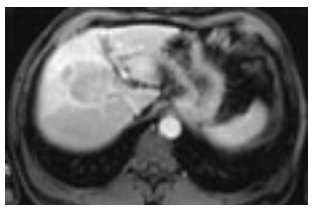


Fig.1a: Contrast enhanced MRI before treatment with DEB TACE showing a solitary HCC in the right lobe

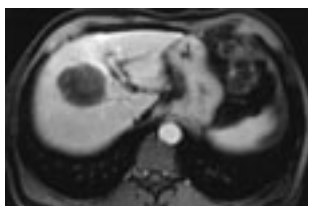


Fig.1b: Contrast enhanced MRI after treatment with DEB TACE revealing complete tumor necrosis

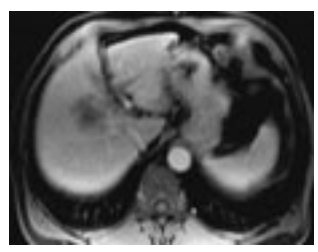


Fig.1c: Contrast enhanced MRI at 6 months follow-up after DEB TACE demonstrates significant reduction in tumor size consistent with partial using RECIST

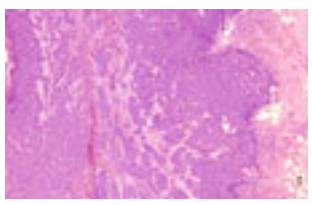


Fig.2a: Magnified view on pathology of VX2 liver tumor before Intra Arterial infusion of 3-Br-Pa

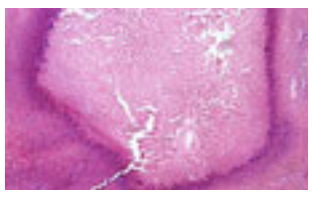


Fig.2b: Magnified view on pathology of VX2 liver tumor after treatment with Intra Arterial infusion of 3-BrPa showing complete cell death

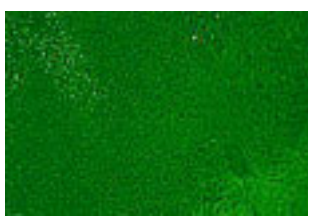


Fig.2c: TUNEL assay of VX2 liver tumor before treatment with Intre Arterial infusion of 3-BrPa reveals viable tumor

Fig.2d: TUNEL assay of VX2 liver tumor after treatment with Intra Arterial infusion of 3-BrPa demonstrates wide spread tumor cell apoptosis

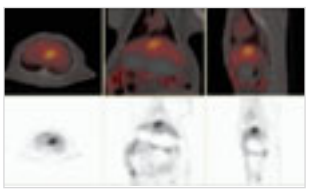


Fig.3a: FDG-PET CT of Rabbit liver with VX2 tumor before treatment with Intra Arterial infusion of 3-BrPa

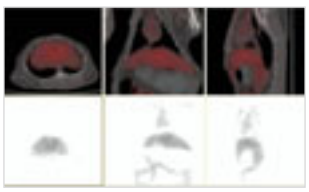


Fig.3b: FDG-PET CT of Rabbit liver with VX2 tumor after treatment with Intra Arterial infusion of 3-BrPa

Drug eluting chemoembolization: Current issues in hepatocellular carcinoma

Don't miss it !
How I do chemoembolization
Workshop
Tuesday, September 22, 17:00-18:00
Room 1.15

Katerina Malagari
Associate Professor of Radiology
Mary Pomoni
Radiology Consultant
Imaging and Research Unit
Dimitrios Kelekis
Professor of Radiology
Director of the Imaging and Research Unit

University of Athens, Greece

The interventional group of the Imaging and Research Unit of the University of Athens has implemented the treatment of HCC with drug eluting beads - first using DC Bead™ ™(Biocompatibles, UK, Terumo) - at 2004. Since then, more than 250 patients with HCC have been treated by this group which has published 2 clinical trials and participated in the Precision V randomised trial comparing conventional chemoembolization with embolization using doxorubicin loaded DC Bead.

Drug eluting particles used in chemoembolization of liver cancer allow both the development of ischemia (vessel occlusion) and the cancerous cell toxicity due to local elution of the chemotherapeutic.

Drug eluting agents currently available for clinical use include the DC Bead™ (Biocompatibles, UK, Terumo) and Hepasphere™ / Quadrasphere™ (Biosphere Medical, Rockland MA S.A).

Until recently, the main bulk of published basic research coming from DC Bead™ has shown that transarterial chemoembolization (TACE) with drug eluting particles/beads (DE – TACE or DEB – TACE) achieves higher intratumoral levels of the chemotherapeutic compared to conventional TACE (c-TACE), and allows prolonged contact time with cancer cells, since the chemotherapeutic is slowly released from the beads that are trapped within the neoplastic vascular network (1-5). In addition, as shown in animal and also in human pharmacokinetic studies with DC Bead these high intratumoural concentrations of the chemotherapeutic do not result in diffusion of chemotherapeutic in the systemic circulation as opposed to c-TACE in which high local concentrations are achieved at the expense of high levels in the peripheral blood, causing systemic toxicity (5-8).

DC Bead™ loaded with doxorubicin achieves a sustained continuous release of doxorubicin for a period of 14 days after injection (3-8). The rate of elution of doxorubicin at the tumour depends on the osmolality of the tumour and the size of the injected beads (the larger the beads, the slower the local release) (3-6). The highest plasma concentrations measured by Poon et al. (52.8±41.5ng/ml) in the DC Bead™ group were 17-fold lower compared to levels measured after administration of 50 mg of doxorubicin in the conventional chemoembolization (900 ±300 mg/ml) (7). Similarly, in the first human study with doxorubicin -loaded DC Bead™ in patients with hepatocellular carcinoma Varela et al. measured concentration of doxorubicin in plasma post embolization and compared with conventional TACE (c-TACE); doxorubicin Cmax and AUC were significantly lower in DC Bead-TACE patients (78.97 ± 38.3 ng/mL and 662.6 ± 417.6 ng/mL min) than in c-TACE (2341.5 ± 3951.9 ng/mL and 1812.2 ± 1093.7 ng/mL min, p = 0.00002 and p = 0.001, respectively) (8).

Lower rates of doxorubicin – related complications were recorded in a recent large Phase II randomised clinical trial comparing c-TACE with DC Bead™ TACE (Biocompatibles, UK, Terumo) (DC Bead was loaded with doxorubicin); the study demonstrated that the adverse events associated with doxorubicin were higher with c-TACE ($p<0.0001$) (8). Liver toxicity with development of liver failure was similarly less frequently seen in the DC Bead™ group compared to c-TACE.

Phase I and II clinical studies with DC Bead™ have proven feasibility, safety, efficacy in the treatment of non resectable HCC (7-10) ; local response in Varela et al. study was 75% (66.6% on intention-to-treat) (8). The mean diameter of the lesions treated was 4.6 cm, the majority were classified as stage Okuda I (Okuda I/II:26/1). Similarly with loaded DC Bead™ Malagari et al., including larger tumours of 3-10 cm in diameter (mean 6.2), report overall complete necrosis in 15.5%, while objective response ranged from 66.2% to 85.5% across four treatments (9).
In addition, the results of a large multicentre randomised trial comparing DC Bead™ –TACE to c-TACE have demonstrated 52% and 63% disease control for c-TACE and DC Bead™ TACE respectively (10) while the rate of complete response was 22% and 27% for c-TACE and DEB DC Bead™ TACE, respectively (10). Including patients with larger tumours (sum diameters of 10.0±5.8) Poon et al. observed 50% objective response at one month after the first treatment (complete response: 0%; partial response: 50%) by RECIST criteria and 70% (complete response: 6.7%; partial response: 63.3%) by the modified RECIST -EASL criteria (7). These results are higher compared to response rates in prospective conventional chemoembolization studies which report 16-35% (10-12).

Hepasphere /QuadrasphereTM (Biosphere Medical, France) presents similar kinetics, being able to absorb doxorubicin or epirubicin within 30 minutes for 90% loading and at 98% at two hours (12,13). Animal experiments at Johns Hopkins University carried out by Kwang-Hun Lee et al, working with Hepaspheres /Quadraspheres™ loaded with doxorubicin in a Vx-2 liver tumour, showed over 90% tumour death at 7 days post treatment compared to 60% death with bland Hepasphere /QuadrasphereTM of the same diameter. Similar results are reported by Gupta et al who in the Vx-2 tumors in rabbits found that intratumoral doxorubicin fluorescence around the spheres was detectable at 1, 3 and 7 days after embolization (14).

Using loaded Hepaspheres and including small lesions ranging from 20mm to 100mm in diameter (mean 42.5mm) and using RECIST with the EASL amendments Grosso et al reported complete response in 48%, partial response in 36% and no cases of disease progression in 1-month follow up (15). At 6 months complete response in the same study was reported in 51.6%, partial response in 25.8% and progressive disease in 22.6%. With Hepaspheres /Quadraspheres™) Kalva et al from Massachusetts General Hospital (16) in their study with14 patients at 3 months reported 50%, 43% and 7%, objective response (OR), stable disease (SD) and progressive disease (PD) respectively. At 6 months OR was 44% and SD 56%.

The ability of the hepaspheres to load with other chemotherapeutics is of great interest. Poggi et al. showed that oxaliplatin can bind with hepaspheres entirely, with a concentration 20 times higher than extra-tumoural liver concentration without major adverse events (17). In their study they report 53.3% stable disease using the RECIST criteria.

Published survival data on TACE performed with drug eluting spheres/beads are limited until now; with DC Bead after a median follow-up of 27.6 months Varela et al. report a 1 and 2 year survival of 92.5% and 88.9%, respectively (8). Similarly, in the study of Malagari et al. survival was 97.05%, 91.1% and 88.2% at 12, 24 and 30 months, respectively (9). No published data are yet available on survival with Hepasphere/Quadrasphere (abstract of Kalva et al reports 74% and 54% for 6 and 12 months respectively (16).

Regarding the choice of particle size, DC Bead increase in diameter is negligible in vivo (3,4). For Hepasphere Gupta et al in the Vx-2 rabbit model used spheres of 50-100μm in the dry state and showed that they increase to 200-400μm after hydration (14). De Luis et al in a porcine model (18) measured the diameter of HepaSphere post kidney embolization and found that 50-100 μm spheres expand to 230.2 +/- 62.5 in the hydrated in vivo state (18). In addition, Bilbao et al in a porcine model comparing the results of kidney embolization between Hepasphere , Beadblock and Contour found that embolization was more distant with the first two agents (19). For DC Bead it has been shown that the smaller the diameter of loaded beads the higher the diameter of necrosis around the injected material (5). Clinically, larger diameters of DC Bead were used by Varela and Poon' s studies (above 300μm) without increased complications, while in the study of Malagari et al. diameters of 100-300μm and 300-500μm (the smaller range of diameters available in DC Bead) were used without complications associated to inadvertent embolization (7,9). The smaller diameters reaching 100μm today are available in DC Bead and shortly in Hepasphere. Safety at this level of diameter has to be reassessed in future studies as fatal complications have been reported in the use of small particles (less than 100μm) if an arteriovenous shunt is overlooked (11).

Inclusion criteria of DEB TACE are similar to those of c-TACE: patients with documented HCC, class BCLC B, good Karnofky score, with relatively preserved liver function (Child-Pugh score A or B). The Precision V randomized study comparing DC Bead™ embolization to c-TACE showed that beads larger than 300μm are safe to use even in multifocal and bilobar disease (when procedures are staged treating one lobe at a time), provided there is no thrombosis of the portal vein (10).

The standardising potential of DEB/DE - TACE is also important for combined treatments with antiangiogenesis agents. In June 2007 a large randomised, double-blind, placebo controlled, multicentre, phase III SHARP trial (n = 602) using sorafenib in patients with advanced HCC (82% BCLC stage C) reported a 44% improvement in median survival from 7.9 to 10.7 months and a median time to radiologic progression of 5.5 months in the sorafenib group and 2.8 months in the placebo group ($P<0.001$)(18). With this evidence, comparison with DE/DEB TACE is currently being investigated.

Currently, randomised studies investigating the potential advantage of TACE combined or not with sorafenib are being performed. In this respect an effective, reproducible, safe procedure of embolization with less complications and adverse events, such as drug eluting TACE, is most suitable in order to be able to identify a specific patient group that would benefit from combined treatment.

Current issues on DE -TACE still have to be studied, including long term survival, histology data in humans from patients that undergo resection or transplantation, the precise role of DE-TACE as neo-adjuvant procedure in patients undergoing resection or transplantation, quality of life, progression rates, time to progression and the most appropriate treatment schedule and repetitions.

In conclusion, DE/DEB TACE clinical studies show that a) treatment offers good local response rates, and b) as the study of Precision V showed: results are better in Child Pugh B disease compared to conventional TACE, while DC Bead™ TACE presents lower complication rates without systemic toxicity. In addition, drug eluting beads provide a model device for the controlled and precise local delivery of chemotherapy intra-arterially (standardised technique). The development of preloaded beads with specific concentrations of chemotherapeutic per ml of hydrated beads would be a further step to better standardise drug eluting TACE.

References:

1. Liapi E, Lee KH, Georgiades CC et al . (2007) Drug-eluting particles for interventional pharmacology.Tech Vasc Interv Radiol 10(4):261-9.
2. Kettenbach J, Stadler A, Katzler IV et al (2008) Drug-loaded microspheres for the treatment of liver cancer: review of current results. Cardiovasc Intervent Radiol. 31(3):468-76.
3. Hong K, Khwaja A, Liapi E, et al. (2006) New intra-arterial drug delivery system for the treatment of liver cancer: preclinical assessment in a rabbit model of liver cancer. Clin Cancer Res 12:2563-7.
4. Lewis AL, Gonzalez MV, Lloyd AW, et al. (2006) DC bead: in vitro characterization of a drug-delivery device for transarterial chemoembolization. J Vasc Interv Radiol 17:335-42.
5. Lewis A. L., Taylor R. R., Hall B., et al. (2006) Pharmacokinetic and Safety Study of Doxorubicin-eluting Beads in a Porcine Model of Hepatic Arterial Embolization. J. Vasc. Interv. Radiol. 17(8):1335 – 43.
6. Namur J, Wassef M, Millot J-M et al. Doxorubicin eluting beads for liver embolization: Pathological findings and correlation with drug distribution in tissue. Abstract 109, 35th Annual Meeting and Exposition of the Controlled Release Society, New York 12-16, July 2008
7. Poon RN, Tso WK, Pang RWC, et al. (2007) A Phase I/II Trial of Chemoembolization for Hepatocellular Carcinoma Using a Novel Intra-Arterial Drug-Eluting Bead Clinical Gastroenterology and Hepatology 5:1100–1108
8. Varela M, Real MI, Burrel M et al. (2007) Chemoembolization of hepatocellular carcinoma with drug eluting beads: efficacy and doxorubicin pharmacokinetics. J Hepatol. 46(3):474-81.
9. Malagari K, Alexopoulou E, Chatzimichail K et al. (2008) Transcatheter chemoembolization in the treatment of HCC in patients not eligible for curative treatments: midterm results of doxorubicin-loaded DC Bead™Abdom Imaging 33(5):512-519
10. Lencioni, R. Malagari K., Vogl T., et al A Randomised Phase II Trial of a Drug Eluting Bead in the Treatment of Hepatocellular Carcinoma by Transcatheter Arterial Chemoembolization Journal of Vascular and Interventional Radiology 2009 Abstract No. 182:(Vol. 20, Issue 2, Pages S70-S71)
11. Brown K. (2004) Fatal pulmonary complications after arterial embolization with 40-120μm tris – acryl gelatin microspheres J Vasc Interv Radiol 15:197-200
12. Osuga K, Khankan AA,Hori S, et al (2002)Transarterial Embolization for Large Hepatocellular Carcinoma with Use of Superabsorbent Polymer Microspheres: Initial Experience J Vasc Interv Radiol 13:929–934
13. Hori S, Okada A, Sakamoto K, et al. (1996) A new embolic material: superabsorbent polymer microsphere and its embolic effects. Jpn J Intervent Radiol 11:375–381
14. Gupta S,Wright KG, Van Pelt CS et al (2006). Hepatic arterial embolization with dosorubicin loaded superabsorbent polymeric microspheres in an animal model Investig Radiol 42 (6):516-521
15. Grosso M, Vignali C, Quaretti P, et al .(2008)Transarterial chemoembolization for hepatocellular carcinoma with drug-eluting microspheres: preliminary results from an Italian multicentre study. Cardiovasc Intervent Radiol 31(6):1141-9
16. Kalva S.P., Dave B., Akbar A., et al Chemoembolization with Doxorubicin-Eluting Microspheres for Inoperable Hepatocellular Cancer: Initial Results Journal of Vascular and Interventional Radiology 2008 Abstract No. 347: (Vol. 19, Issue 2, Pages S127-S128)
17. Poggi G, Quaretti P, Minoia C, Bernardo G (2008) Transhepatic arterial chemoembolization with oxaliplatin-eluting microspheres (OEM-TACE) for unresectable hepatic tumours. Anticancer Res. 28(6B): 3835-42
18. de Luis E, Bilbao JI, de Ciércoles JA, Martínez-Cuesta A, de Martino Rodríguez A, Lozano MD. In vivo evaluation of a new embolic spherical particle (HepaSphere) in a kidney animal model. Cardiovasc Intervent Radiol. 2008;31(2):367-76.
19. Bilbao JI, de Luis E, García de Jalón JA, de Martino A, Lozano MD, de la Cuesta AM, Sangro B. Comparative study of four different spherical embolic particles in an animal model: a morphologic and histologic evaluation. J Vasc Interv Radiol. 2008;19(11):1625-38
20. Llovet JM, Real MI, Montana X, et al. (2002) Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. Lancet 359:1734–9.

Portuguese Delicacies

(other than Cristiano Ronaldo)

Petra Mann
CIRSE Office

Here are the five reasons why you will love Lisbon while being here and hate it every time you go to the gym for at least a year:

Pastéis de Nata, or as I like to call them: Deliciogasms
You cannot leave Lisbon before trying a pastel de nata! I have to warn you, though: if you try to avoid being seen in public drooling all over yourself (at least until retirement), they might not be right for you, as they are bound to make you lose control of several facial muscles, giving you an expression of heavenly bliss only high-impact calories can induce.

The best place to get a pastel de nata is the Fábrica dos Pastéis de Bélem, a beautiful 19th century store where people will step over each other to get to Lisbon's most delicious treats (wear elbow protectors!). It was there where I was told that a pastel de nata only had 122 calories, which, although very unrealistic, I choose to believe, so I must ask you to keep your knowledge about metabolism to yourself at this point.

Legend has it that the monks of the adjacent Jerónomo monastery invented the delicious treats. Why is it that monks always discover the best food stuffs? Well, I guess we have to thank the Vatican for celibacy at this point. Apparently the Fábrica dos pastéis de Bélem's recipe for the popular treat is one of Portugal's best kept secrets which can only be known by seven people at a time. You just have to love a country that gives this kind of importance to pastry!

Before eating your patel de nata, cover it with cinnamon first and icing sugar second (1-2 cm should do)

Olives
If you ask me (and who wouldn't?), Portuguese olives are by far the best in the world. They are milder than the ones from Greek, yet more flavourful than the Spanish ones. In most restaurants they are served as a freebee before meals and even people who are not big olive fans will find themselves devouring them by the fistfuls. Due to the fact that they are often pickled with garlic and other spices, they might not make you particularly successful with the other sex that evening, but on the bright side mosquitoes will stay away from you, too.

Port wine
Port wine is one of Porgual's most delicious treats. The typically sweet red wine also comes in dry, semi-dry and white varieties and is only produced from grapes grown and processed in the Douro region. Due to its high sugar and alcohol content (19.5-20%) you should not have too much of it, though, as you might wake up in the middle of the street, only wearing a fedora and vaguely remembering that you have promised one of your kidneys to a bum. Not that that has ever happened to me.

Port wine is aged in wooden barrels. Hence the term a "barrel of fun", I suppose.

A sandwich soaked in beer – makes a BLT look pretty weak, huh?

Francesinha
A francesinha is probably the craziest concoction you will ever try (unless you joined a fraternity at some point). It consist of a sandwich baked with cheese on top (still fairly standard, you may say) and then – here it comes – served in a sauce made of tomato paste and beer. Yes, men of this planet, it has been done. A sandwich has been soaked in beer and is waiting for you in a bar here in Lisbon.

Now that I have reduced my readership by at least 50% I can tell you ladies what you probably already know - that through the cooking of the sauce there is of course no alcohol left in the dish. Although it is a specialty of Porto, it can be found in cafés and bars in Lisbon as well and should be sampled, if not for anything else, at least out of scientific interest.

Bacalhau
Portugal has a coast line of almost 1,800 km. It therefore comes as no surprise that it has Europe's highest fish consumption per capita, the bacalhau (cod fish) being by far the most popular one. It is served in such a vast variety of ways that according to a proverb you could have bacalhau every day of the year without ever repeating a recipe. Foreigners will ask why on earth anyone would want to do such a thing, but the Portuguese seem to think it perfectly reasonable.

IR Congress News is published as an additional source of information for all CIRSE 2009 participants. The articles and advertorials in this newspaper reflect the authors' opinion. CIRSE does not accept any responsibility regarding their content.
If you have any questions about this publication, please contact us at mann@cirse.org.

Editors in Chief: *Afshin Gangi, Paulo Vilares Morgado*
Managing Editor: *Petra Mann, CIRSE Office*
Graphics/Artwork: *LOOP. ENTERPRISES media / www.loop-enterprises.com*

Booth 27

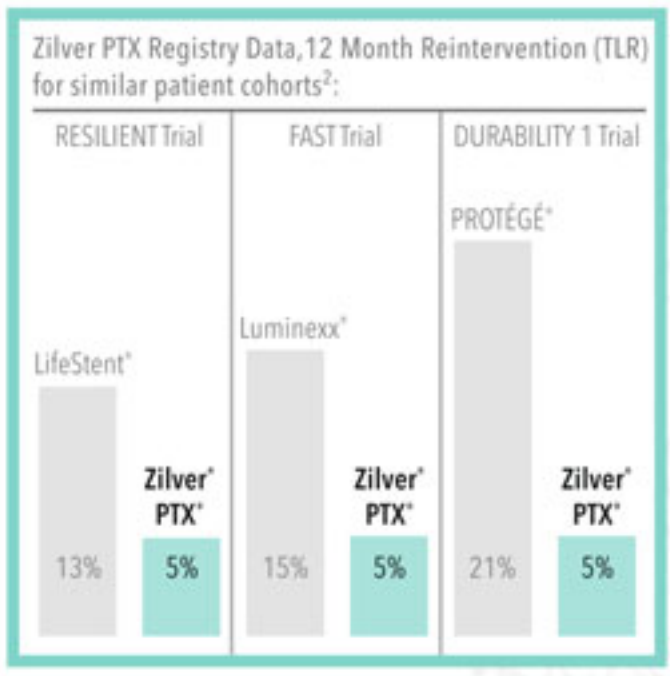
100% POLYMER-FREE DRUG DELIVERY

INTRODUCING:
The world's first drug-eluting SFA stent **Proven** to reduce risk and reinterventions

The Zilver PTX (paclitaxel) drug-eluting stent blocks cell proliferation that can lead to restenosis, while eliminating the unnecessary polymer that may cause long-term problems. In fact, Zilver PTX has been proven to reduce reintervention[1] rates in the SFA (superficial femoral artery) by 50% when compared to other leading stents.[2] Now you have a tremendously powerful weapon against peripheral arterial disease.

Visit cookmedical.com/zilverptx to learn how Zilver PTX can raise your standard of care.

Cook Medical–Advancing Leg Therapies worldwide.



References:
1. Target lesion revascularization (TLR): clinically driven reintervention for ≥ 50% DS within treated segment (included ± 5 mm); surgical bypass of target vessel. 2. Dake M. Interim analysis of two-year results for the Zilver PTX drug-eluting peripheral stent. Presented at: 2009 Vascular Annual Meeting; June 11-14, 2009; Denver, CO. *LifeStent and Luminexx are registered trademarks of C.R. Bard, Inc. PROTEGE is a registered trademark of EV3 Peripheral, Inc.*

COOK MEDICAL

Zilver® PTX®

DRUG-ELUTING PERIPHERAL STENT

AORTIC INTERVENTION | CARDIOLOGY | CRITICAL CARE | ENDOSCOPY | INTERVENTIONAL RADIOLOGY | PERIPHERAL INTERVENTION | SURGERY | UROLOGY | WOMEN'S HEALTH