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ECIO 2015
Sixth European Conference on Interventional Oncology
April 22-25
Nice, France

THE REVIEW

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With interventional oncology expanding at a rapid rate, keeping pace with the latest developments and incorporating them into your daily practice can be a challenge. ECIO 2015, held in Nice from April 22-25, provided an excellent opportunity for practitioners engaged in cancer care to update themselves on the most recent research results, techniques and technical advances.

The meeting was a huge success, attracting over 1,300 delegates from 68 countries, with Nice providing a beautiful backdrop for the event.

Highlighting cutting-edge research

A cornerstone of this year’s event was the interesting research being carried out in the field, with the new Best IO Papers session introducing studies that are shaping the future of cancer care. Presented research included studies comparing doxorubicin-eluting beads to conventional chemoembolisation for HCC; exploring the use of sunitinib-eluting beads for chemoembolisation; comparing partial nephrectomy and ablation for cT1 renal masses; comparing survival outcomes of sub-lobar resection and thermal ablation for early-stage non-small cell lung cancer in older patients; and a closer look at percutaneous long bone cementoplasty of the limbs.

Promoting interdisciplinary cooperation

Patients now benefit from a vast array of specialist knowledge, but effectively pooling that knowledge to optimise care can be challenging. To encourage more effective interdisciplinary collaboration, several Multidisciplinary Tumour Boards were once again offered, bringing together experts from different specialties, including hepatology, surgery and interventional radiology, to jointly analyse individual cases. The sessions underscored that experts often agree on how to proceed, but that they are also able to offer unique insights based on their various perspectives. The referring physician programme is another important element of CIRSE’s efforts to reach out to other disciplines. We were delighted to once again welcome a diverse group of professionals, including gastroenterologists, oncologists, surgeons, radiation oncologists, as well as nurses and radiographers, to the meeting.

Open cooperation also involves working with diverse partner societies on joint sessions. This year’s programme featured sessions organised in collaboration with the Japanese Society of Interventional Radiology (JSIR), the European Society for Medical Oncology (focusing on colorectal liver metastases), and the World Conference on Interventional Oncology (addressing molecular oncology and translation into the clinic).
Scientific highlights in 2015

With over 40 hours of scientific education being offered, it is difficult to single out the highlights. The Honorary Lecture delivered by Yasuaki Arai, JSIR President and Director of the National Cancer Center in Tokyo, had some surprising insights on establishing an effective evidence base for IO procedures, and the true goal of the interventional radiologist. The four hands-on workshops again offered participants an invaluable training opportunity, while the Video Learning Sessions walked delegates through complex procedures in a step-by-step fashion.

To get a flavour of what clinical advances were discussed, please find a more detailed review of selected sessions overleaf...
The Fundamentals of Oncology

A clinical focus session dedicated to the fundamentals of oncology placed the procedures performed by interventional radiologists engaged in cancer care into a broader context, and addressed challenges encountered in the pursuit of evidence on the effectiveness and safety of the various therapies used, underscoring the importance of clinical involvement.

Prof. Sandrine Faivre (Lausanne/CH) provided a broad introduction to conventional chemotherapy. The main classes of agents involved in colorectal cancer include alkylating agents, which interact with the DNA of tumour cells to impair their proliferation; anti-metabolites, such as 5-FU, which integrate into the DNA molecule; and anti-topoisomerases, which target the DNA’s repair enzymes. By contrast, taxanes, a more recent class of agents, interact with microtubules, inhibiting their depolymerisation. The main side effects include myelosuppression, which may manifest as neutropenia, which increases the risk of infection. Prof. Faivre noted that, for advanced colorectal cancer patients, survival rates were limited to six months before chemotherapy was introduced. Today, especially when combined with targeted therapies, survival extends beyond two years. Dr. Faivre also indicated that for chemo-sensitive disease, chemotherapy is the main systemic treatment for advanced stages, and is used as an adjuvant therapy for localised stages after surgery. She also emphasised that chemotherapy effects require radiological evaluation every three months.

Prof. Faivre’s second lecture focused on targeted therapy, which relies on scientifically designed drugs to block relevant biological tumour targets. For advanced HCC, not considered chemotherapy-sensitive, Sorafenib, a VEGFR-inhibitor, is the only medical therapy approved as a first-line treatment. For liver metastases from colorectal cancer, which is chemo-sensitive, two agents are mainly used in combination with chemotherapy: an anti-proliferative agent (cetuximab) and an anti-angiogenic agent (bevacizumab). The safety profile of targeted therapy differs from that of chemotherapy, with skin and vascular toxicity mainly observed. Complications can include necrosis and bleeding; while rare, this can be potentially severe. Finally, the efficacy of combining targeted therapies with IR techniques (ablation, TACE and RE) has not yet been validated outside of trials, and such an approach does increase the risk of adverse reactions. Additional trials are needed to properly gauge the risks and benefits.
Dr. Eric François (Nice/FR) outlined the **differences between Phase I, II and III clinical trials**. Phase I studies represent the first administration of a new drug (or a new combination of drugs) to humans. In the oncological context, no healthy volunteers are included, and the studies are generally proposed to patients who have no hope of improvement with traditional treatment. The main objective is to determine the recommended dose for future trials. Phase II trials, the most common in oncology, seek to demonstrate sufficient efficacy in specific clinical situations, with an acceptable tolerance profile. Phase III trials, which include both superiority and non-inferiority trials, aim for both tolerance and efficacy. Phase IV studies occur post-approval, and seek to analyse results in real practice, including detecting rare and/or late toxicities. While the scientific level of these trials is not very high, they can provide very useful data for clinical practice.

Prof. Riccardo Lencioni (Pisa/IT) discussed **defining response in interventional oncology trials**, focusing on HCC. The goal of oncological treatments is to improve survival, and, for the past fifteen years, this has been evaluated by means of the RECIST criteria, which focus on tumour shrinkage. This approach does not work in interventional oncology, which induces necrosis, a development not paralleled by changes in tumour size, at least not in the early follow-up stages. Five years ago, modified criteria, known as mRECIST, were implemented. These introduced the concept of a “viable” tumour, and outlined recommendations for image interpretation of HCC in cirrhosis, which involves changes that can result in incorrect determinations of progression. Mostly scrutinised in the context of TACE thus far, mRECIST appears to better capture changes in tumours that have clinically meaningful implications. However, it is still of limited use for purposes of comparing results of clinical trials.

Dr. Riad Salem (Chicago, IL/US) explained **how endpoints in interventional oncology may differ from medical oncology trials**. He outlined the clinical and radiological endpoints generally used for trials involving interventional oncology, noting potential differences between endpoints with local therapies and systemic therapy. He then explained how typical IO endpoints (PFS, local recurrence rate) are defined, and discussed their validity in oncology.

*Presentations are available at [www.esir.org](http://www.esir.org)*
The Quest for Evidence

For many years, interventional radiologists have been devising creative ways to treat various cancer-related complaints. However, for these treatments to move from the realm of theory into clinical acceptance, evidence is needed: safety must be demonstrated, efficacy must be established, and finally, the procedure must be compared with existing therapies, in terms of both clinical outcomes and costs.

This remains one of the major challenges facing interventional oncology. However, progress is being made, and a number of sessions outlined the advances being made on this front, as well as identifying the very real limitations facing IO.

Honorary Lecture

Strengthening IR’s evidence base has been a major priority for Yasuaki Arai, director of the National Cancer Center Hospital in Tokyo, throughout his distinguished career. In 2002, he set up the Japan Interventional Radiology in Oncology Study Group explicitly to facilitate pursuing evidence on minimally invasive cancer care. However, in his Honorary Lecture, Dr. Arai – considered one of the founders of interventional oncology – urged the medical community to look “beyond the evidence”.

Dr. Arai acknowledged that identifying the most suitable treatment option largely involves making choices after considering the probabilities of success based on scientific data. He further noted that, in evidence-based medicine, a treatment option supported by evidence becomes the standard, and that doctors generally provide the standard treatment to patients. With interventional oncology’s role in cancer care still limited, he emphasised, evidence is in fact the discipline’s best weapon.

But evidence-based medicine has its limits, Dr. Arai continued, and established evidence represents only the tip of the iceberg. Noting that medical oncologists often inform advanced-cancer patients that no
recommended treatment is available for them, he stated that he found this frustrating, and, as an interventional oncologist, has a different approach. He then outlined several situations in which he offered risky options, not strongly backed by evidence, to patients suffering from advanced cancer who had previously been told they were out of options. He stressed that, where patients fully understand the risks involved, this can be the best way to proceed, and described how these risky procedures ended up greatly enhancing the patients’ quality of life or significantly prolonging their survival.

Therefore, as important as evidence is, and as much as it should be respected, it is not always enough for proper patient care. Dr. Arai urged physicians to move away from always insisting on previous evidence, and to instead challenge themselves to think about all possible ways to provide better treatment, using their knowledge, techniques and ideas. This, he explained, is what he means when he emphasises that it is important to move “beyond the evidence”.

Dr. Arai further noted that clinical trials within IO can be especially challenging: with imaging systems, equipment, techniques and skill-levels often varying, results for a specific procedure used to treat the same disease can greatly differ. He added that these difficulties could largely be overcome by standardising IO procedures, and by using the standard endpoints used in oncology, especially when evaluating new IO techniques.

Finally, Dr. Arai noted that another main challenge remains for the IO community: cost. Deeming this the most important global issue confronting medicine, he stated that, even where a standard is based on evidence, it cannot become a global standard if it cannot be applied in small or remote centres around the world. Developing new treatments is important, he acknowledged, but making available treatments accessible to a broader patient population is even more precious.

The Best IO Papers

To reflect the growing wealth of research being done, a new session was established in which some of the most influential IO papers published in 2014 were presented by the authors. This proved enormously popular, and very informative.

The first paper presented was *Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses* (Thompson et al). Co-author Dr. Thomas Atwell (Rochester, MN/US) explained that the study identified 1,803 patients from the prospectively maintained Mayo Clinic Renal Tumor Registry, and observed that recurrence-free survival was similar for PN and ablation patients, while metastases-free survival was superior for PN and cryoablation patients when compared with RFA. Overall survival was superior after PN, likely because of selection bias.
Percutaneous long bone cementoplasty of the limbs: experience with fifty-one non-surgical patients (Cazzato et al), was introduced by Dr. Jean Palussière (Bordeaux/FR). For poor surgical candidates, at 1-month follow-up, percutaneous long bone cementoplasty (PLBC) proved to be safe and effective, with pain palliation more significant for lesions of the upper limb. If cement stress fracture occurs following PLBC (9% of cases), surgical external fixation is still an affordable therapeutic option.

Sunitinib-eluting beads for chemoembolization: methods for in vitro evaluation of drug release was presented by lead author, Katrin Fuchs (Geneva/CH). This Swiss study assessed three in vitro release methods for their potential to predict slow in vivo release of sunitinib from chemoembolisation spheres to the plasma, and fast local in vivo release obtained in an earlier study in rabbits.

The outcomes of the Precision Italia Study Group’s paper, Randomised controlled trial of doxorubicin-eluting beads vs. conventional chemoembolisation for hepatocellular carcinoma, were discussed by lead author Dr. Rita Golfieri (Bologna/IT). 177 patients were randomised one-to-one to undergo cTACE or DEB-TACE and followed for at least two years or until death. DEB-TACE and the cTACE were shown to be equally effective and safe, with the only advantage of DEB-TACE being less post-procedural abdominal pain.

Lead author Dr. Sharon Kwan (Seattle, WA/US) presented the SIR-sponsored paper, Thermal ablation matches sublobar resection outcomes in older patients with early-stage non-small cell lung cancer, which compared survival outcomes. After controlling for selection bias, this study found no difference in overall survival between patients treated with sublobar resection and thermal ablation.

Quality pays: clinical excellence saves money

Afshin Gangi (Strasbourg/FR) opened the session by examining whether structured IO reporting can improve quality without adding cost. Structured reporting may reduce the incidence of errors and make it easier for referring physicians, billing specialists, medico-legal representatives and researchers to work with. It can be an effective education tool for trainees, and help establish a standard lexicon. Systematic reporting is especially useful in complex areas, but there are concerns that it could kill creativity, and lead to incomplete and inflexible reporting styles.

However, the option exists to create a flexible structure: Prof. Gangi felt that a report with defined headers, but free text (albeit with a standardised lexicon) could work well within IR, and greatly enhance efficiency and quality. These would have to be customised to individual procedures, and should include items such as patient information and history; consent; indications; procedural information, including anaesthesia; technical aspects and devices; immediate results and complications;
after-procedural care; clinical imaging and follow-up protocol; and conclusions. For certain procedures, diagrammes could be included, as is currently being done by the European urology societies to great effect.

The origins and evolution of clinical care pathways were discussed by Alban Denys (Lausanne/CH), who also assessed whether introducing these in the IR field could improve quality without adding cost. There are a number of terms to describe such pathways (care plans or maps, patient pathways), and they refer to a group of methods and instruments for care management of a well-defined group of patients, within a well-defined period of time. While the primary goals can vary, the most common aims are to improve quality of care, reduce risks, increase efficient use of resources, and increase patient satisfaction.

It is difficult to evaluate the exact impact of such pathways, but evidence from the stroke sector indicates that they increase the number of radiology exams and the length of stay, but lead to less readmission, better patient documentation and lower hospital costs overall.

Prof. Denys detailed the steps needed to introduce such pathways, and his own hospital’s ongoing experience. A full-time project manager is needed, which represents a financial commitment, but the benefits of doing so (which includes a reduction in turf battles and improved efficiency) means that it is a worthwhile investment.

To provide background information on cost-effectiveness in patient care and how to measure it, special guest speaker Paul McCrone (London/UK) gave an economist’s perspective. He pointed out that no matter the healthcare model, resources are always scarce: there is always a limit, but patient demand increases exponentially, due to aging populations, technological advances and high expectations. Decisions between the competing alternatives must be made.

Thus far, very few economic evaluations have been carried out in interventional oncology. While patient pathways are dictated largely by needs, an economic evaluation is based largely on outcomes generated by input. These may analyse different endpoints (cost-minimisation, cost-benefit, cost-effectiveness, cost-consequences or cost-utility analyses). Economic evaluations are not solely about reducing costs; they also seek to maximise outcomes, and counter-intuitively, increasing investment may prove to be cost-effective.

Gathering data can prove a challenge – trials are complex, lengthy and expensive. However, he underscored the importance of collecting service use and quality-of-life data (certainly within any trials being run, but also observational data). Other options open to IRs include making use of administrative databases and developing simulation models. Such information would allow more accurate judgements to be made when deciding resource allocation.
Radiation oncologist Lizbeth Kenny (Brisbane/AU) discussed **disinvestment in medicine, and the need for evidence**. While the term disinvestment is perceived very negatively, it is a necessary part of ensuring that resources are delivered in a way that maximises patient outcomes. This, argued Dr. Kenny, should be more actively embraced by the medical community, as leaving the decision-making to administrators will lead to dissatisfaction amongst patients and clinicians alike. It also opens the door to reinvestment.

In order to benefit from reinvestment, IO must provide quantitative evidence showing itself to be as good as or better than other therapies, with a lesser overall economic burden and a better quality of life. CIRSE is currently very engaged in producing guidelines, and Dr. Kenny urges that this be expanded to this to deliver QALY or cost-benefit evidence.

Level 1-based guidelines are often not real-world situations. The oncology world generally needs to refocus on what is meaningful to the patient, in terms of benefit, tolerability and of course, economic viability. Local treatments such as RT or thermal ablation provide excellent outcomes, and she urges the IO community to begin demonstrating this, and leading the way in investment philosophy.

The science underpinning IO was addressed by Riccardo Lencioni (Pisa/IT): **how should we prove the value of what we do?** Ten years ago, the SIR IO Task Force published their vision for the future. This predicted that research in the field would lead to significant discovery and clinical implementation of novel and effective cancer therapies, and that the field would become accepted as a “fourth pillar” of cancer care. Sadly, the evidence produced in the intervening years has not met that demand.

Some good data has been gathered, particularly in the HCC field, but the level of evidence gathered does not meet the current standards. Randomised controlled trials (double-blinded too) are needed. Acknowledging that the rapid evolution of devices poses a challenge in embarking on lengthy and expensive trials, Prof. Lencioni nonetheless urged adoption of ASCO recommendations for raising the bar. Some examples of how this could work in practice were given, but echoing Dr. Kenny, he put forward the idea that different assessment endpoints might be needed, in order to demonstrate the value of IO therapies.

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Despite progress with respect to detection, diagnosis, surveillance and treatment, hepatocellular carcinoma is the third leading cause of cancer deaths. Presentations outlined trends and accomplishments, identified remaining hurdles, and highlighted the myriad ways interventional radiology contributes to the increasingly multidisciplinary fight against liver cancer.

**Early-stage HCC**
Prof. Valérie Paradis (Clichy/FR) addressed the pathology of early HCC, focusing on tumours smaller than 2 cm. Advances in imaging techniques and screening protocols for high-risk populations have led to better detection of small nodules, but differentiating between pre-malignant nodules, such as high-grade dysplastic nodules, and early HCC, and between early and progressed HCC, remains challenging. Biopsies can be particularly helpful, both for differential diagnoses and to provide prognostic indicators, and cooperation between pathologists and radiologists is essential to properly analyse both macro- and microscopic tumour patterns.

Dr. Christoph Zech (Basel/CH) tackled imaging of early HCC. Where patients suffer from either cirrhosis or longstanding viral hepatitis, and imaging shows hyper-vascularty and washout, imaging can suffice. MRI is especially useful, thanks to diffusion-weighted imaging and the use of tissue-specific contrast media. However, vascular criteria have limitations, and imaging alone does not always resolve the diagnosis, meaning a biopsy is necessary. Once early HCC is diagnosed, accurate staging is crucial for treatment purposes, particularly with cure a possibility. Dr. Zech noted that all imaging technologies can have difficulties with lesions smaller than 1 cm, and identified MRI with hepatobiliary contrast imaging as a significantly superior technique.
Dr. Nisar Malek (Tübingen/DE) discussed **why and how to biopsy**. Where imaging is not characteristic, and a tumour is smaller than 2 cm, a biopsy should be performed (with tumours larger than 2 cm, second imaging suffices). Biopsies can also help estimate the risk of HCC formation in cirrhotic livers, and, with small HCC, provide additional genetic information that assists physicians in making correct diagnoses. Moreover, tissue analysis can help predict recurrence following curative treatment, and should become a standard part of treatment. Biopsies can also facilitate predicting a patient’s response to treatment, and could play an important role in guiding future, more individualised care.

Dr. Pietro Majno (Geneva/CH) addressed transplantation waiting lists. The medical community has expressed concern about drop-outs, with many urging that transplants be performed sooner, or bridging treatments used. Dr. Majno maintained that recurrence is a bigger problem, and that simply observing patients during the wait is an often-overlooked option that makes sense in certain cases. While bridging treatments – limited to TACE or RFA for early HCC – have shown to be effective for patients facing waiting times between 6 and 18 months, he questioned their value for T2 patients who have to wait less than six months, as well as for T1 patients. Deciding when to delist patients is an important question, and better data is necessary to answer it.

Prof. Riccardo Lencioni (Pisa/IT) reviewed the **evidence on resection vs. ablation** for early HCC. Randomised controlled trials so far preclude clear comparisons, but studies on very small tumours (average of < 2.5 cm) have demonstrated that the two are equally effective. For patients who qualify for resection but suffer from a solitary, small tumour, ablation and resection are both good curative options (with tumour location a vital parameter); and for patients precluded from resection, ablation is the best option, though response rates will not be as high where tumours reach 5 cm. However, individual discussions of cases remain important. Furthermore, truly improving long-term outcomes requires tackling recurrence, and research on novel drugs and molecular-targeted therapies in adjuvant settings, following resection or ablation, should be a priority.

**Intermediate-stage HCC**

Dr. Riad Salem (Chicago, IL/US) assessed the **BCLC and HKLC systems for HCC**. The BCLC has been widely used for clinical trials, and recommended by Western scientific societies for clinical practice. However, it has been criticised for oversimplifying HCC and for being too conservative. The Hong Kong staging system refined stratification by tumour number, size and PVT; introduced the concept of locally advanced tumours; and created a unique stage for certain transplantable early HCC. It also reflects a more aggressive approach, emphasising surgery in intermediate and advanced disease and endorsing RFA for lesions larger than 5 cm. However, the system requires further validation. This necessitates adapting local practice, which is controversial.
identifying patients beyond BCLC A who might benefit from ablation will remain more of an art than a science.

Prof. Thomas Helmerger (Munich/DE) scrutinised drug-eluting beads versus conventional TACE. Current practice focuses on one liquid agent (Lipiodol) and several particulate agents, both bland and drug-eluting. Drug-eluting beads entail a low drug concentration in plasma and a higher or longer concentration in the tumour. Vascular complications are rare, but non-vascular complications are quite common. Research suggests these occur somewhat less frequently with DEB-TACE. While TACE has evolved, and DEB-TACE may be superior to the classic approach, demonstrating statistically significant improvements in survival rates remains elusive, and there is no consensus on the optimal technique.

Dr. Eveline Boucher (Rennes/FR) addressed radioembolisation for intermediate HCC. Dividing BCLC stage B into four sub-categories based on CPT score, liver status and tumour load, she endorsed the therapy for BCLC B3 patients (with impaired liver function) and BCLC B2 cases (especially with large and multifocal tumours), and as an alternative to resection for BCLC B1 patients who do not qualify for surgery for general reasons. She noted that radioembolisation can be performed in an outpatient setting, and can be adapted to the tumour load, but acknowledged that TARE is new, entailing a high learning curve and risk of adverse events; that it requires true cooperation between units; and that it is expensive.

Dr. Patrick Chevallier (Nice/FR) addressed the role of ablation in intermediate HCC. With monopolar RFA linked to high recurrence, modifications are clearly necessary. Options include increasing the ablation area, but the few studies available indicate that even a large security margin around the main tumour may not prevent recurrence in case of local invasion. Combining RFA with another therapy is also an option. Under certain circumstances, combining TACE and RFA can be beneficial for patients with either a single lesion of 3-5 cm or multiple within the Milan criteria. However, more solid scientific proof is needed. In the meantime,
Dr. Rodolphe Anty (Nice/FR) outlined the current evidence regarding *systemic therapy in intermediate HCC*, noting that the heterogeneity of tumours and variety in molecular pathways add considerable complexity. Sorafenib is effective in BCLC C and B patients, and, in practice, is offered to patients who do not qualify for TACE, or for whom TACE fails. Recent efforts focus on using Sorafenib to optimise TACE, but meta-analyses of this approach have yielded contradictory results, and results of a new randomised Phase III study comparing Sorafenib and DEB-TACE to DEB-TACE alone are pending. Finally, at this point, no clear evidence supports using Sorafenib as adjuvant after either resection or ablation.

**Colorectal liver metastases**

In a joint session with ESMO, Dr. Marc Peeters (Edegem/BE) stated that the ultimate goal of *personalised medicine in oncology* is sufficiently defining the disease to enable identifying and treating only those patients most likely to respond. It focuses on using biomarkers to help predict treatment safety and/or outcome efficacy. Technological advances are also leading to the use of gene panels, but the medical community needs to determine whether the information suffices to justify clinical changes. Reorganisation is also needed as pathologists switch from routine pathology to molecular pathology. In addition, personalised medicine involves more multidisciplinary teams, which can be challenging. Finally, managing the costs of all the new information and technology is also crucial.

Prof. Jean-Yves Douillard (St. Herblaim/France) indicated that most CRCLM patients are fit to receive *systemic therapy*, but that this decision should be made by a multidisciplinary team. Available cytotoxic agents include three main groups (Fluoropyrimidines, Irinotecan and Oxaliplatin), as well as the rarely-used Raltitrexed. It is also possible to add two categories of biological agents to chemotherapy (anti-angiogenesis and anti-EGFR). For patients with resectable metastases, perioperative chemotherapy provides modest, non-significant improvement, but for patients with potentially resectable metastases, downsizing by way of chemotherapy does result in 5-year survival rates similar to initially resectable patients. However, most patients encountered are unresectable, and chemotherapy is used to extend survival, control symptoms and preserve quality of life.
Dr. Christoph Zech (Basel/CH) noted that the growth in therapeutic options has rendered assessing tumour response after TACE/SIRT more complicated. Although traditional approaches (the RECIST criteria and volumetry) still dominate, new functional approaches show promise. Perfusion MRI remains insufficiently standardised, but PET-CT is faring better, and could be very useful in gauging overall survival based on early response. However, it is vital for physicians who review follow-up examinations to be aware of the possible variety in imaging findings, including an increase in size and other unexpected findings that must be correctly interpreted.

Prof. Michel Ducreux (Villejuif/FR) outlined the rationale and indications for hepatic intra-arterial delivery of chemotherapy in CRCLM, which places a high level of concentration into the metastases without resulting in too much systemic spread, preventing toxicity. Several drugs can be used, including 5-fluorouracil and a potential game-changer, Oxaliplatin. Intravenous administration will always remain simpler. Also, the literature on the arterial approach has not shown improved overall survival. However, Oxaliplatin, a new drug, is promising, even in patients resistant to intra-venous administration of the drug. Combining HAI of Oxaliplatin with chemotherapy (cetuximab) has also yielded good results. In patients who undergo resection, adjuvant administration of HAI after surgery shows positive results in terms of recurrence-free survival, but again only with Oxaliplatin. Efforts to produce Phase III trial results are underway.

Prof. José Ignacio Bilbao (Pamplona/ES) detailed study results on radioembolisation in CRCLM, including the SIRFLOX study, which compares SIRT with FOLFOX to FOLFOX alone as a first-line treatment for non-resectable CRCLM. Initial results from March 2015 show no statistically significant improvement in progression-free survival at any site. However, adding SIR-Spheres Y-90 resin microspheres to a chemotherapy regimen did show such a statistically significant improvement in PFS in the liver compared to chemotherapy alone. Two other studies, FOXFIRE and FORXFIREGlobal, should shed further light on the issue, but results will not be available for another year.
Managing complications
Dr. Shaun Samuels (Miami, FL/US) explained that major complications from TACE include hepatic failure, hepatic abscess/biloma, cholecystitis and death, then outlined three situations in which he and other interventional radiologists encountered difficulties. His advice for preventing complications included avoiding a “macho mentality” by refraining from pushing the limits of one’s therapy; letting a surgeon get involved where necessary; with respect to HCC, being aware of the variety in feeding vessels; and consulting colleagues.

Dr. Patrick Chevallier (Nice/FR) discussed digestive complications following RFA in the liver. Colonic perforation, while infrequent, is always associated with morbidity, as well as death in up to 40%. Typically discovered 5-8 days after RFA, it usually requires surgery. It can generally be prevented by colonic insulation; contraindicating patients is recommended where colonic protection is not possible. Gastric perforation is another complication; its frequency is unknown and symptoms vary. Associated with severe morbidity, it can and should be prevented through heat insulation.

Prof. Carmen Ayuso (Barcelona/ES) also addressed complications following ablation, including bleeding into the liver, the most common direct complication; portal vein thrombosis, caused by heat damage; liver infarction; extra-hepatic organ injuries; and liver failure, which is most commonly encountered in cases involving prior hepatectomy or with cirrhotic patients. Prof. Ayuso also summarised the results of a Japanese survey of over 13,000 patients, reporting a mortality rate of 0.038%, and major complications with 3.54% of nodules.

Dr. Andreas Mahnken (Marburg/DE) focused on complications following radioembolisation, asserting that post-radioembolisation syndrome, a common adverse event, should be considered a side-effect. Other risks include hepatic dysfunction, hepatic fibrosis and portal hypertension, radiation choleystitis and radiation-induced cholangitis. Mahnken outlined several challenges encountered, including duodenal ulceration, which, after radioembolisation, can only be successfully treated with proton pump inhibitors in about 50% of patients; other anti-inflammatory treatments show promise, but currently remain experimental.

Other sessions
A multidisciplinary tumour board brought together a hepatologist, interventional radiologists and a surgeon to analyse five cases involving HCC. The experts agreed almost entirely on how to proceed, but were able to offer unique insights based on their various perspectives.

Finally, a video-learning session also focused on liver treatments, with experienced physicians explaining how they perform various percutaneous procedures, covering liver ablation and venous occlusion, combined cTACE and ablation, DEB-TACE, Y-90 and PVE.

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Musculoskeletal applications were addressed in a number of sessions, including a Hands-on Workshop, Interactive Sessions and even a Video-Learning Session. Evidence for their use was presented alongside radiotherapeutic and surgical options at the Clinical Focus Session, equipping those practicing MKS interventions with the skills needed to be clinically involved in their hospital’s tumour boards.

**Evidence for local control with ablation**

Dr. Matt Callstrom (Rochester, MN/US) discussed the evidence for using ablation to achieve local tumour control in bone and soft tissue. Early results indicate that a number of modalities can be successfully used to target such tumours, and may be particularly useful for tumours that don’t respond well to chemotherapy, such as chondrosarcoma.

Existing data covers a mixed range of histologies (melanoma, renal and others), but the Mayo Clinic experience has achieved 87% overall local control (CI 75-93%). While the disease-free interval is generally short (average 6 months), ablation seems to offer an extended survival of approximately 4 years, shifting the clinical focus to a quality of life issue.

Disease-specific outcomes for three tumour types were addressed in more detail. Oligometastatic prostate cancer responds well to ablation. Cryo-ablation produces a good biochemical response: local control is in the 80% range, with PSA reduction from approximately 1.5 ng/ml to 0.3 ng/ml.

Approximately 65% of RCC patients present with a single site of metastasis, often in lung or bone, which respond well to focal therapy. While cryotherapy is not cheap, it compares well with systemic therapies, and has been recorded as achieving local control of 87%.

Desmoid tumours have a high surgical recurrence (77%) and wide margins are necessary, entailing significant morbidity. Ablation can offer good functional preservation, and is a potential front-line therapy.

**Evidence for radiation therapy in local control**

Radiation therapy (RT) is widely used in MSK treatment, with 50% of all cancer patients receiving it. Dr. Barbara Jereczek-Fossa (Milan/IT) discussed the advances being made in the field, and how improved survival rates have led to a new aim: “cure without complications”.

As primary MSK tumours are rare, there is no Level 1 evidence available. For primary bone lesions, local control of ~90% has been demonstrated in extremity tumours, while spine and pelvis lesions do not respond well to conventional RT. Advances in carbon ions and proton-beam treatments may improve response in radioresistant tumours such as chondrosarcoma and chordoma. Soft tissue tumours predominantly appear in extremities (50%) and trunk (33%). RT is an intrinsic part of limb preservation, and in combination with wide-excision, has largely replaced amputation, with grade A recommendation (5-year local control >80%, 5-year OS 50-60%).
Bone and soft tissue metastases are a common cause of severe cancer pain. RT is given routinely, as it confers pain relief in 60-90% of patients.

RT offers many advantages: it is a pain-free, non-invasive outpatient procedure that is easily combined with other modalities. However, it does have its limitations, and IR options may help bridge this gap. Advances in oncology are moving us towards chronic or even chronic curable cancer, and the better-tolerated local treatments will play a strong role here.

**When does HIFU fit in?**

Delivered under US or MR guidance, high-intensity focused ultrasound is totally non-invasive, does not involve ionising radiation, and has low complication rates. Dr. Alessandro Napoli (Rome/IT) discussed the evidence for its use in MSK settings.

RT is the gold standard for bone metastases, but up to 30% of patients may remain with painful lesions at the end of treatment. As a result, two centres in Rome and Bologna have designed a prospective, single-arm, multi-centre study. So far, 72 patients with 87 non-spinal lesions and VAS ≥4 have been enrolled. While not complete, individual cases show great promise, and Dr. Napoli gave some impressive examples that delivered immediate and dramatic pain relief. Clinical experience thus far indicates that not only can MRgFUS be used as primary technique in pain palliation; it has a potential role in achieving local tumour control.

Osteoid osteoma is another interesting application: a small number of cases achieved good results when the nidus was targeted. Dramatic pain relief was conferred with 24 hours, and patients remained stable at 18- or 24-month follow-up. The safe, non-invasive and repeatable nature of HIFU means this should be considered as a primary technique in treating osteoid osteoma.
Bone consolidation: cementoplasty vs. osteosynthesis

Dr. Frédéric Deschamps (Villejuif/FR) described the role of cementoplasty and percutaneous osteosynthesis, focusing on the consolidation applications of both. Cementoplasty is particularly suited for compression fractures of the vertebrae, but cement leakage from high-pressure areas is a constant concern, and to protect against this, filling should be stopped before optimal consolidation is achieved.

Consolidation of the pelvis or proximal femur raises other challenges. Bone cement is not appropriate for tension or shear stress, and fractures frequently occur despite consolidation in e.g. the femoral head, pubis, iliac crest and acetabular roof. Leakage through fracture lines is again a consideration. To overcome both, percutaneous screw fixation can be employed. The procedure is similar to a biopsy, and requires an 8 G needle, a Kirschner wire and cannulated screws. It can be performed under fluoroscopy, but 3D acquisition is needed to assess placement. One drawback of screw fixation is that metastasis growth can displace the screw. In such cases, combined use of screws and cement is a good option.

Bone palliation and consolidation are major issues in cancer patients. Cementoplasty is well-established, but has limitations. Screw fixation is a straightforward procedure that achieves both consolidation and pain relief, and must be considered as an additional tool in the therapeutic arsenal of all IRs.

When to use embolisation in combination with ablation

Little evidence exists to support combined use of embolisation and ablation, but the topic was tackled with gusto by Dr. Anthony Ryan (Waterford/IE), who also addressed various technical considerations.

Use of pre-operative embolisation predates ablative technologies. Initial studies demonstrated safety and efficacy. One of the few RCTs in the field (Clausen et al) demonstrated a significant reduction in operating time, and reduced blood loss in hypervascular tumours. The sooner surgery follows embolisation, the greater the reduction in blood loss, as with time, recanalisation and collateral establishment occurs. It can be presumed that similar mechanisms apply to ablation, although this remains to be proven. Palliative embolisation works primarily by virtue of decreasing tumour volume and turgor, and has a knock-on effect of decreasing compression of adjacent structures. It has not yet been established if there is a synergistic effect with ablative techniques.

Dr. Ryan detailed the outcomes of various small series. While none can give us a definitive answer, there is weak evidence to show benefit when combined with other therapies. Based on this, he believes that embolisation is generally underutilised, and that it complements ablative outcomes. It is a safe procedure, and can be a powerful tool for palliation, but more data is needed.

Presentations are available at www.esir.org
In recent years, ECIO has witnessed an increase in the number of speakers and sessions addressing pulmonary cancers, both primary and metastatic. Unsurprisingly: lung cancer accounts for 12% of all cancer cases, and is the leading cause of cancer death. As the pool of case reports grows, so the indications for its use are growing ever clearer.

This year’s congress offered valuable advice on patient selection and optimal delivery, and offered a range of interactive, hands-on and video-learning sessions, alongside traditional lectures.

Evaluating lung function

Prof. Charles Marquette (Nice/FR) explained the dire outcomes for lung-cancer patients: it has a 5-year survival rate of <15%, and only complete resection of early-stage disease can be curative. Surgery, however, can only be offered to fewer than one in four patients, due to late-stage diagnoses and associated co-morbidities.

85-90% of cases are tobacco-related, and thus associated with other diseases: 50-90% of these patients have underlying chronic obstructive pulmonary disease, and 15-20% underlying coronary heart disease, both of which may be contra-indications for surgery. Pre-operative evaluation is thus crucial, and a delicate balancing act between reducing the cancer burden and preserving lung function is required.

To evaluate pulmonary function, forced expiratory volume (FEV1) and gas exchange capacities (DLCO) should be measured; several low-tech tests can also be used, such as the staircase test (ability to climb 6 floors = low risk; 2-3 = high) or the shuttle-walk test (>400 low risk; <250 high). Post-operative predictions of function should then be calculated using pre-operative FEV1 values × (1−Y/Z) [where Y=number of functional segments to be removed; Z=total number of functional segments].
For those deemed at moderate or high risk, Dr. Marquette’s experience indicates SBRT or RFA, although a proper evaluation of possible complications (such as pneumothorax, bleeding or exacerbation of interstitial pneumonia) and contra-indications (coagulation disorders, dyspnea at rest, unstable cardiac condition, performance status III or IV) is mandatory.

**Surgery in lung metastases**

Thoracic surgeon Prof. Bernward Passlick (Freiburg/DE) gave an excellent overview of the criteria for curative resection of metastases, and the surgical options available.

Currently, uni- or bilateral, sequential or simultaneous thoracotomy are widely employed, with much debate about the value of video-assisted thoracic surgery (VATS), which risks missing additional metastases: a retrospective analysis of pre-operative CT findings at the University of Freiburg showed that for presumed single-lesion patients, additional lesions are found perioperatively in 7%, rising to 27% for patients with multiple lesions. Caution is thus advised for all pursuing minimally invasive treatments in multiple-metastatic patients. For single metastases, there appears to be no difference in long-term survival outcomes between VATS and thoracotomy.

Wedge resection is widely used (70% of cases). It is a straightforward procedure, but some additional lung tissue is always lost if a stapler device is used. Anatomical resection (<10% patients) and dissection of lung tissue is also commonly performed.

Especially exciting are the technical improvements of pulmonary laser surgery: wavelength modifications allow for a quick and very precise resection, entailing minimal blood loss. It can be used for multiple lesions; deep lesions can be sutured in a sequential, multi-layered fashion with resorbable materials. This procedure will result in initial scarring, which may be confused with recurrence on CT, so additional care is required at follow-up.

Lots of variables determine how many metastases can or should be resected, including location, primary tumour type, lung function, co-morbidities and therapeutic alternatives.

Prognostic factors include the primary tumour (germ cell tumours show excellent response, but only account for 4% of primary cancers), disease-free interval and complete resection: the number of metastases does not seem so important. In a systematic review, 5-year survival for single lesions was 54%; for multiple metastases 37%; for normal CEA 43%; and for elevated CEA 22%. Prof. Passlick concluded by restating the tissue preserving benefits of laser-supported metastatectomy, and stressed that therapy decisions are best made in a tumour-board setting.
Ablation as a first-line therapy?

Dr. Alice Gillams (London/UK) gave a brief overview of the indications and protocol for performing pulmonary ablation, before outlining the safety profile and clinical outcomes. Pneumothorax is a common occurrence, with an incidence similar to that associated with lung biopsy (overall 40%; requiring drain insertion 10%; resulting in more than 24-hour hospitalisation <1%).

An important advantage of ablation is its ability to preserve lung function. The preservation of parenchyma is of particular importance to patients who are likely to have multiple metastatic episodes, as it maximises the treatment choices at each stage of the disease.

Dr. Gillams then compared the treatment options for colorectal lung metastases: surgery is unproven, has limited indications and a 5-year survival of 38-60%; chemotherapy can reduce lesion size, but complete eradication is unlikely; SBRT is suitable for 1-2 lesions, but requires fiducial insertion, and is limited in the size and locations it can treat. The data for ablation compares well: three 2015 series on lung metastases demonstrated a 3-year survival rate of 64, 44 and 76%, respectively. These and other studies show that smaller tumours respond better and, in line with the surgical data presented by Prof. Passlick, that the number of lesions is not as important as previously thought.

For sarcoma patients particularly, ablation may have a lot to offer: 40-80% develop intrapulmonary recurrence post-resection, and chemotherapy offers a median survival of just 12-18 months. Not only is RFA a minimally invasive, readily repeatable procedure, but a 2013 study of 22 patients (55 lesions of 0.5-2 cm) achieved primary local tumour control of 95%, an overall mean survival of 51 months, and 2- and 3-year survival of 94% and 85%. Size < 1cm, number (solitary or multiple), uni- or bilateral, prior surgery or chemotherapy, and trunk vs. extremity primary tumours did not impact survival.

The literature for other tumour types is not so well established. Small series show some benefit – for example, oesophageal and nasopharyngeal ablation achieve outcomes similar to surgery. One study of RFA for RCC metastases (de Baère) demonstrated a five-year survival of 53.8%. Dr. Gillams concluded that ablation represents a safe, effective and repeatable treatment for lung metastases, and should be the first-line option for lesions ≤ 3.5 cm.

Imaging follow-up

The optimal imaging schedule to use after surgery, SBRT and ablation was presented by Prof. Robert Suh (Los Angeles, CA/US).

Multiple therapeutic options currently exist for the treatment of both primary and secondary pulmonary malignancies, and reliable and diligent
imaging follow-up is essential. Dr. Suh outlined the expected findings for each modality (resection, metastasectomy, conventional RT, stereotactic RT, radiotherapy and RFA), as well as projected timelines for when follow-up should be performed.

Knowledge of CT and FDG-PET patterns is critical for early identification of tumour recurrence and progression. Operators should be diligent in identifying the pathological completeness of therapy, any confounding inflammatory effects of therapy, and the biological activity of the disease. CECT and PET should be used in conjunction.

**Evidence from comparative trials**

Dr. Lorenzo Monfardini (Brescia/IT) gave an overview of the existing comparative data for treating pulmonary metastases.

Surgical literature most commonly addresses colorectal metastases (17 studies; 1,684 patients). 5-year survival is 41-56%, and the mortality rate is < 2.5%. The best surgical candidate has a prolonged disease-free interval between the primary and metastatic lesions; normal CEA; no nodal involvement; and a single metastasis. Spirometric changes after pulmonary metastasectomy are affected by the total volume of lung parenchyma resected: the functional loss after 3 or more non-anatomical resections is comparable to that recorded after lobectomy.

The multicentre RAPTURE study (2008) examined RFA in 73 metastatic patients who were unsuitable for surgery, radio- and chemotherapy. Overall survival at two years was 66% for CRM and 64% for other metastases, respectively. In 2013, a 122-cohort study indicated that RFA might be a suitable alternative to surgery for small peripheral tumours. A recent paper (de Baère et al, 2015) demonstrated an overall survival rate of 51% at 5 years, as per major surgical series, and excellent respiratory function outcomes.

Comparing these with SBRT is more difficult – as the “youngest” technique, follow-up data of just two years is available. A 2010 systematic review of SBRT in 175 lesions in 148 patients demonstrated a local control rate of 78.6% at two years. The overall survival at two years was 50.3% (33-73%).

Lack of Phase III trials make it impossible to determine which therapy is best – the real question, to Dr. Monfardini’s mind, is which therapy to use first. Using overall survival, rather than disease-free survival, as a primary marker, and considering the option of reintervention, he would currently recommend ablation as the first choice for treating small pulmonary metastases.

*Presentations are available at www.esir.org*
While a number of image-guided interventions are now being used with curative intent, palliation and pain management remain an important part of cancer care for all oncology professionals. Interventional radiologists have much to offer patients, and various aspects of symptom management were discussed throughout the congress, as well as at a dedicated Clinical Focus and Video Learning Sessions.

Opening the session on symptomatic cancer treatment, Dr. Liz Kenny (Brisbane/AU) discussed the evidence-base of radiation therapy for pain, one of the most feared aspects of a cancer diagnosis. The most common scenarios where radiotherapy is considered for pain relief are bone pain, local infiltration by cancer, local compression of structures, nerve root pressure or liver metastatic pain. In treating liver metastases, 20-30 Gy improves pain in 75-90% of patients, and affords complete relief in 50%.

Bone pain is the most common scenario for patients being referred for RT, which is one of the most effective and widely used strategies. Such pain can be cancer-related (mass effect on adjacent structures; inflammatory cytokines), but structural integrity can also be compromised, meaning a combined approach is needed. A 2011 Cochrane review of RT for bone metastases determined that while single and multiple fraction achieve similar pain palliation (60% improvement; complete relief 32-34%), but that single treatments were associated with a much higher retreatment and almost double the fracture rate.

More experimental RT treatments are also being pursued. Single large ablative doses have been employed for spinal metastases. Weak evidence for radionuclides shows only small benefit, and that severe adverse events are common. Targeted agents such as 131I, 177Lu and Denosumab (although not an RT drug) are useful.

Dr. Kenny stressed that knowing your limitations is critically important. RT is highly effective at relieving tumour-related pain (as well as being safe and inexpensive), but does not work for all patients and does not immediately relieve structural pain. RT should always be strongly considered for cancer pain, in a multidisciplinary setting, as part of the full armamentarium for bone metastases.
The use of nerve blocks was presented by Dr. Georgia Tsoumakidou (Strasbourg/FR). Current guidelines prioritise the use of opioid therapy for pain management, but despite the use of these, many cancer patients still suffer pain, and these patients may benefit from IR procedures. These can be divided into two categories: direct action (thermal ablation, embolisation, cementoplasty) and indirect action (nerve blocking).

Nerve blocks can be performed using thermal (cryoablation or RFA) or chemical neurolysis. Chemical blocks can be temporary (local anaesthetic; often used as a “trial run”) or permanent (ethanol or phenol), resulting in the intentional destruction of a nerve to interrupt pain impulse transmission. They are generally performed in the sympathetic chain (coeliac plexus, splanchnic nerve most common) for visceral pain that is resistant to other therapies, or more rarely in spinal nerves.

Alcohol (50-96% solutions) is the most widely used agent, and is effective for up to four months. Injection causes pain, and local anaesthetic should always be used concomitantly. Phenol (concentration 7-12%) produces a shorter-lasting, less intense blockage than alcohol, with slower diffusion. Other agents include glycerol and hyper-/hypotonic solutions.

While nerve blocks can be effective, they are not without risks and side-effects, and careful consideration of the patient’s needs and prognosis is required before proceeding. Direct action should be favoured, with nerve-blocking used as a last resort for severe pain management.

Dr. Pierre Bize (Lausanne/CH) addressed the percutaneous treatment of pleural effusion. There are five types of fluid that can be present in the pleural cavity (serous, blood, pus, urine, chyle), and a distinction is usually made between transudate (when hydrostatic pressure increases) and exudate (inflammation-increased vascular permeability), most commonly caused by malignancy.

Asymptomatic presentation requires observation, but for symptomatic pleural effusion, thoracentesis can be performed either diagnostically or to relieve the patient. It is a straightforward procedure that can be performed under US, providing information in >90% of cases. However, case must be taken to stay above the ribs to avoid vessel damage.

Chest tube drainage dates back to the time of Hippocrates. It is performed under US or CT guidance, using local anaesthetic and the Trocart/Seldinger technique, with the free end of the tube attached to an underwater seal or drainage sac with a fluttering value, to prevent air from entering the pleural cavity. Progressive drainage avoids re-expansion pulmonary oedema, and the tube should be flushed twice a day to prevent clogging.

Pleurodeisis is used to prevent recurrence of pneumothorax or pleural effusion. It can be performed chemically (bleomycin, povidone iodine, talc) or surgically, and requires sufficient pain relief. The chest tube can be removed when drainage <100 ml/day.
Indwelling drainage catheters (e.g. PleurX) allow home-drainage by the patient themselves. It is useful where pleurodeisis fails, or for recurrent pleural effusion. It is important that the patient can care for the catheter themselves, and that no more than 1.5l is drained at a time.

**Percutaneous treatment of malignant ascites** was discussed by Dr. Phil Boardman (Oxford/UK). Only 7-10% of ascites are malignancy-related. The majority of cases are synonymous with development of peritoneal carcinomatosis (half of all patients), but a significant minority of patients will have other causes. Most arise from ovarian or unknown primary tumours. Symptoms include abdominal distention and pain, shortness of breath and early satiety.

US-guided intermittent paracentesis is widely but heterogeneously used, providing >90% symptomatic relief. The outpatient setting is safe, feasible and cost-effective; however, only 12.8% of patients stayed in hospital <12 hours (RCOG findings). Although effective, it is inconvenient and costly in patients with recurrent ascites, for whom longer-term solutions are needed.

Long-term paracentesis is performed via tunneled indwelling silicone catheters with an external one-way valve. Devices are vacuum-assisted or employ free drainage. They offer repeated flexible drainage in the community, lower costs, and better symptom control due to more frequent, smaller drainage. As these patients are generally nearing the end of life, Dr. Boardman generally leaves the follow-up to the community care team, to minimise hospital attendance. Most problems, he noted, are generally due to logistics and communication, rather than the catheters themselves.

Peritone-venous shunts are best suited to active individuals with good performance and cardiovascular status. Passive flow is position-dependent (supine optimal) and occurs at a gradient of >3 cm H2O. Literature focuses on technical feasibility with little outcome data. The choice between indwelling catheter and PVS is largely a matter of local and patient preference.

*Presentations are available at [www.esir.org](http://www.esir.org)*
Expert Course

The Future of Image-Guided Tumour Ablation – Targeting Techniques and High-End Clinical Strategies

Innsbruck (AT), December 11-12, 2015

This course brings together seasoned interventional radiologists to scrutinise the latest image-guidance systems and ablation methods. The primary goals are identifying technologies that hold the most potential for positive results, determining their most effective deployment, and specifying possible refinements.

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New Horizons

Throughout the meeting, presentations detailed the current status of myriad ablation procedures, introduced new areas of application, and outlined various recent insights in molecular oncology, providing an intriguing glimpse into the future of oncological care.

Ablation: current status and future horizons

Multiple ablative modalities are available, Dr. Brad Wood (Bethesda, MD/US) noted, but radiofrequency ablation entails several benefits, including that it is time-tested, with more long-term data available. Results are comparable to resection for small (< 5 cm) HCC in overall and disease-free survival. In addition, RFA is predictable at the tip, cauterises better than cryoablation, and its “slow cooking” can be advantageous. Promising developments include combination therapies (with TACE, XRT and drugs), and advancements in immunotherapy, with an “RFA vaccine” holding the potential to dramatically change cancer care. The modality is also being extended to new organs, including the prostate, pancreas and breast.

Prof. Nahum Goldberg (Jerusalem/IL) provided a detailed update on electroporation. The drawbacks of standard techniques used to treat small, solid tumours (such as RF, MW and cryoablation) include heat-sink effects and potential damage to adjacent structures. Electroporation entails no heat-sink effect and has limited impact on the bile duct. However, it requires general anaesthesia and cardiac monitoring. Predictability is also an issue: more research is clearly required. However, where other techniques are not suitable, IRE shows potential for use in previously untreatable disease, especially pancreatic cancer and liver tumours in difficult locations.

Prof. Philippe Pereira (Heilbronn/DE) addressed microwave ablation. Devices now feature high-power and internally cooled antennae, as well as thermal, field and wavelength controls. For liver tumours smaller than 3 cm, RFA and MWA produce similar results. Research also indicates that local recurrence rates for HCC and colorectal cancer hepatic metastases are significantly better with microwaves. MW also entails less heat-sink effect, less perfusion-mediated cooling, and faster heat generation, which allows better treatment of liver tumours near large vessels. In addition, it is a good option for lung tumours because of the limited heat conductivity of pulmonary tissue.
Dr. Irene Mindjuk (Dachau/DE) discussed HIFU. MR-guidance offers exact tumour location, the ability to avoid critical structures thanks to visualisation of the treatment zone, and real-time thermometry for therapy control. US-guidance is more frequently used and entails lower costs, but is highly operator-dependent. Clinical applications have expanded. Uterine fibroids are one of the best-developed indications, and technological improvements have reduced skin burns. In Europe, HIFU is also approved as a first-line treatment for bone metastases, primary benign and malignant bone tumours, multiple myeloma and facet joint syndrome. The evidence on its efficacy for prostate cancer is still limited. Applications in neurosurgery are promising. However, more RCTs are needed.

Dr. David Breen (Southampton/UK) views cryoablation as underused, especially in Europe. Many centres resist cryo because it involves large Argon and Helium tanks, but companies are predicting “tank-less” cryoablation by late 2016. Other efforts include producing thinner probes, which now have shaft insulation to prevent skin burns. Cryo’s main benefit is cryo-lesion conspicuity. In addition, the ablation zone appears to fade faster than with RFA. Cryoablation shows particular strength in bone tumour ablation, pain palliation for malignant bone disease, adrenal ablation, and chest wall disease. There is some debate as to its role in focal prostatic disease.

Dr. Martin den Brok (Nijmegen/NL) discussed combining immunomodulation with ablation. Immunologists are exploring an in vivo dendritic cell (DC) vaccine, which requires both antigen-loading of DC in vivo and maturation of DC in vivo. The former is done via in situ tumour destruction. Several ablation techniques, especially cryoablation, have been investigated. Researchers are now turning towards HIFU; mechanical ablation shows particular promise, completely destroying cell structures. In terms of DC maturation, combining ablation with CpG, a synthetic nucleotide sequence, greatly benefits immunity. It has become clear that even greater immunity results when ablation is combined with immune stimulating complexes (ISCOMs); the researchers now plan to test combining CpG and ISCOMs.

**Ablation: expanding the boundaries**

Dr. Jung Hwan Baek (Seoul/KR) addressed RFA for benign thyroid nodules. Korean guidelines identify three indications: symptomatic problems, cosmetic problems, or hyper-functioning nodules related to thyrotoxicosis. The procedure involves local anaesthesia, and guidelines recommend two techniques (the trans-isthmic approach and the moving-shot technique). Clinical outcomes for patients with symptomatic problems entail a volume reduction of around 50% at one month, of 90% at one year, and the effect was maintained throughout the 4-year follow-up. Complications include voice change, haematoma, vomiting, skin burn, brachial plexus injury and nodule rupture, as well as abscess formation and hypothyroidism.
Dr. Jean Palussière (Bordeaux/FR) presented ablation for small breast malignancies, an option thanks to ever earlier detection. The literature deals mostly with breast cancer in the elderly. RFA results so far indicate good long-term efficacy. However, there is a risk of failing to detect the occult microscopic extent of the tumour; continuous follow-up, preferably with MRI, is essential. The ablation zone often remains palpable, requiring clear communication with the patient; there is a risk of scarring skin burns; and, in the long term, nipple retraction may occur. Cryo is less painful, can be performed under local anaesthesia, and can treat lesions both larger and closer to the skin.

Prof. Constantinos Sofocleous (New York, NY/US) discussed adrenal tumour ablation, an option when surgery is not possible, or in case of recurrence after resection. It requires general anaesthesia and continuous arterial blood-pressure monitoring. Reported technical success rates have been very high. For solitary adrenal tumours, results have been particularly good, with one study indicating that half of the patients were cured at a mean follow-up of 29.8 months. Complications are rare, but practitioners must be ready to intervene should a hypertensive crisis due to catecholamine secretion or bleeding occur. Ablation could soon serve as first-line therapy for select smaller adrenal tumours.

Dr. Alice Gillams (London/UK) addressed lymph node ablation, which can be effective, but requires careful patient selection and excellent staging. It is indicated for isolated, loco-regional recurrence, and mostly used when surgical and radiotherapy options have been exhausted. Practitioners must think carefully about potential collateral damage, keeping a 1 cm distance from the edge of the ablation to critical structures. Low-power and short treatment times often suffice. The initial end-point is devascularisation on US, CEUS or CT, with shrinkage or disappearance visible at follow-up.
With prostate cancer caught earlier and a lower proportion of patients presenting with metastases, focal ablation is of increasing interest, noted Dr. David Woodrum (Rochester, MN/USA). Benefits include an attractive side-effect profile; that future surgery and radiotherapy remain possible; and that it may offer a low-risk treatment for patients in the “watchful waiting” category. However, practitioners must make sure they are not inadequately treating patients. Overall, long-term data is lacking. Currently, cancer in the native prostate gland is being treated with MRgFUS, cryo- and laser ablation. US-guidance has also been used, but MRI is superior. For recurring prostate cancer, MR-guided cryo- and laser ablation offer additional treatment options to those who qualify neither for surgery nor further radiation.

Molecular oncology and translation into the clinic

In a joint session with the WCIO, Prof. Goldberg discussed oncogenic pathways and their relevance to interventional oncology. Practitioners must better understand systemic effects triggered by procedures they perform. For example, ablation may influence organ homeostasis, residual tumour growth and tumour initiation. Tackling this requires determining which cytokines induce cellular reactions that occur post-RFA. Research indicates that various cytokines are elevated following ablation, with cytokine IL-6 substantially elevated a week after the procedure. Anti-cytokine drugs may reduce unwanted systemic effects, with research on RFA with adjuvant liposomal anti-IL6 siRNA, for example, showing a significantly reduced tumour growth rate. The issue is not limited to ablation; recent data suggests that TACE can induce pro-oncogenic changes. Successfully manipulating these unintended side-effects requires closer cooperation with molecular oncologists.

Dr. Wood outlined developments relating to tumour hypoxia. Current research efforts are scrutinising the interaction and dynamics of hypoxia, angiogenesis, inflammation and immunomodulation, as well as of Hsp70, toll-like receptors, HIF1a, VEGF, IL-6, stem cells and gene expression. With some tyrosine-kinase inhibitors more effective on hypoxic tumours, integrating rational drug choices is a priority. In addition, imageable drugs hold considerable promise. Other future developments include identifying optimal combinations of various focal, regional and systemic treatments.

Prof. Jens Ricke (Magdeburg/DE) addressed immunomodulation and radioembolisation. The goal is to overcome the immune shielding of tumours. Anti-CTLA-4 and anti-PD-1 (Ipilimumab and Nivolumab) are getting much attention, and have been approved for melanoma to squamous non-small-cell lung cancer. Radiation induces immunologic cell death, thus enhancing or enabling immunologic response. Radiotherapy promotes endogenous vaccination, and immune checkpoint modulators (like CTLA-4 and PD-1 block) outperform immunogenic tumour shielding. When combining immunology and radioembolisation, the less of a tumour load involved, the better the synergy.
Prof. Jeff Geschwind (Baltimore, MD/US) stated that tumour glycolysis is a key hallmark of cancer, and the final common pathway to most, if not all, tumours, making it an interesting target. A number of drugs specifically targeting tumour metabolism are under development. These include 3-Bromopyruvate, which contains the key ingredient of Bromine. Animal studies on intra-arterial delivery of 3-Bromopyruvate in free form showed results as early as two hours following treatment. Subsequent efforts have focused on delivering it systematically, with researchers recently succeeding in doing so by way of nano-molecular microencapsulation, a breakthrough development.

Dr. Rafael Duran (Lausanne/CH) tackled image-guided drug activation. Various hypoxia-targeting therapies have been developed, including hypoxia-activated prodrugs (HAPs), with TH-302 currently the most advanced in clinical development. Its efficacy in systematic delivery has been demonstrated. There might be a synergistic effect when combining conventional chemotherapy with TH-302; this is being explored in various trials, including two Phase III randomised controlled trials. Moreover, HAPs can be used in the interventional oncology setting, with the combination of TH-302 and cTACE recently showing particular promise. However, additional studies are needed.

Prof. Alban Denys (Lausanne/CH) presented efforts to develop a DNA repair inhibitor. Currently available molecules targeting DNA repair pathways all target only one of the two main enzymes involved in the repair. D BAIT, developed by DNA Therapeutics, is a double DNA fragment which, injected systemically or locally, enters cells and acts as an activator of the different molecules. As a result, all enzymes are trapped and can no longer actively repair DNA. Having shown promise in combination with TACE, it could also be combined with ablation systems: research on mice has indicated that D BAIT enhances the effect of RFA. Ongoing research efforts are focusing on different cell lines and variations in injection protocols.

Presentations are available at www.esir.org
Not only do our corporate partners devise, develop and supply the tools needed to treat our patients, they also play an active role in supporting educational events such as the ECIO meeting.

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The annual ECIO meeting offers all physicians interested in image-guided oncological therapies an opportunity to learn about new developments and discuss best practice. Since the early days of image-guided biopsies and palliative stenting, the field has expanded to cover a staggering range of clinical options.

Next year’s meeting, to be held in Dublin, Ireland, will endeavour to cover a broad cross-section of these therapies, focusing on the most recent advances. Under the new chairperson, Prof. Thomas Helmberger, the Scientific Programme Committee has already devised an exciting and varied programme.

**Colorectal liver metastases**
A core theme will be metastatic colorectal liver cancer. More than one million new colorectal patients are seen each year worldwide: approximately 15% of these have liver metastases at diagnosis and around 60% develop these during follow-up. Recent interventional oncology data demonstrate some promising adjuvant therapies, as well as increased survival time and improved quality of life in unresectable patients. These treatments and their clinical application will be thoroughly examined in various Clinical Focus Sessions and a Multidisciplinary Tumour Board.

**A varied programme**
Other topics to be discussed include staples such as imaging, HCC, lung cancers, new developments and the clinical management of patients. 2016 will also feature a dedicated immunotherapy session – an exciting field which deserves the attention of the oncology community. The conference will also address newer clinical territories such as neuroendocrine tumours and cholangiocarcinoma, as well as hosting a discussion on quality assurance in the IO field.

**Join us in Dublin!**
These exciting sessions will take place in the Convention Centre Dublin, the first carbon-neutral convention centre in the world, whose striking glass frontage and curved walls offer the perfect backdrop to a field as dynamic and forward-thinking as interventional oncology. We hope to see you there!
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