RT. In 2009, ESTRO is offering 29 different teaching courses, including special editions organised in developing countries (e.g. several in Asia). ESTRO is also involved in the formulation and (at the moment) updating of European standards for training curricula. To support the scientific advancement of RT, ESTRO organises annual meetings, in even years on its own, in uneven years together with ECCO/ESMO; these years the three other RT disciplines have their own meetings. The ESTRO meetings are truly interdisciplinary, with both dedicated and joint tracks for physicists, biologists and technologists, in addition to radiation oncology tracks. From the 2008 meeting, there have also been dedicated sessions developed by and for young scientists in the field of RT. In addition, ESTRO has been/is involved in the organisation of several tumour site specific meetings (e.g. for head and neck and urological cancer) as well as inter-disciplinary meetings with other medical specialities (e.g. nuclear medicine).
RT is an important treatment modality in the management of cancer. With the many on-going developments in radiation oncology, biology, physics and technology, it is very likely that RT also in the future will remain the major organ-sparing treatment alternative for cancer. In Europe, ESTRO is the key player in this field, providing support for this process through education, training and the advancement of science.

## *Scientific Symposium* (Wed, 23 Sep, 14:45−16:45)
## Liver metastases from colorectal cancer

**245** INVITED

**Radiofrequency ablation, a new standard?**

T. Ruers[1]. [1]*Antoni van Leeuwenhoek Ziekenhuis, Department of Surgical Oncology, Amsterdam, The Netherlands*

**Introduction:** During the past few years techniques on tumour ablation by radiofrequency have evolved significantly. This development resulted in an increasing use of radiofrequency over Europe. Although the technique proved to be safe and was adopted by many institutions, the place of radiofrequency ablation in patients with colorectal liver metastases is still not well defined. Hence, today there is still a clear need for scientific evidence that defines the role of radiofrequency therapy in patients with colorectal liver metastases.
**Technique and devices:** The basic idea behind local tumour ablation is to selectively destruct tumour tissue without significant damage to the remaining liver. RFA can be performed during laparotomy (open), laparoscopy or percutaneously. On line monitoring of the ablative procedure is crucial in order to obtain complete tumour destruction. Ultrasonography is the most commonly method used and allows accurate tumor destruction during open procedures. For percutaneous RFA, both CT and MRI imaging have been reported to be more reliable.
**Local tumour control by RFA:** For lesions smaller than 4 cm local recurrence rates after open RFA procedures (during laprotomy) are generally be reported around 5−7%. For percutaneous RFA comparable results are reported when the procedure is performed under CT or MRI guidance.
**Use of RFA in patients with unresectable colorectal liver metastases:** Chemotherapy is the gold standard for patients with unresetable colorectal liver metastases. From the theoretical point of view, however, local tumour destruction by RFA could be beneficial to those patients with (unresectable) liver metastases only. Despite many reports published so far, it remains difficult to delineate the role of RFA in this patient category. Results published are often confusing by reporting overall treatment results in a wide variety of different tumour types and with many different treatment strategies. It is only until recently that the interim results of a randomized study became available (CLOCC study, EORTC 40004). This phase II study investigates the efficacy of RFA plus chemotherapy versus chemotherapy alone in patients with unresectable colorectal liver metastases. Interim analysis shows that PFS is 16.8 months in the RFA arm versus 10 months in the chemotherapy only arm. When definite analysis confirms these results, RFA becomes an acceptable treatment option in this patient category.
**Use of RFA in patients with resectable colorectal liver metastases:** It is highly likely that with a local recurrence rate of 7%, local tumour ablative procedures like RFA may enter the arena of treatment alternatives for resectable colorectal liver metastases. However at present, patient selection and treatment strategies with combined treatment of RFA plus chemotherapy need further evaluation before RFA may be considered as an equivalent treatment option to resection.

**246** INVITED

**Liver metastases from colorectal cancer. Which staging method is optimal?**

W.J.G. Oyen[1]. [1]*Radboud University Nijmegen Medical Center, Department of Nuclear Medicine, Nijmegen, The Netherlands*

Various imaging modalities for staging patients with metastatic colorectal cancer have emerged or have evolved into powerful tools in the last decade. Multislice CT is still the cornerstone for choosing appropriate treatment. MRI (with or without novel contrast agents) provides better delineation of liver metastases. Furthermore, positron emission tomography (PET) using FDG has has shown that the addition of FDG-PET changes patient management in up to 30% of patients with potentially resectable liver metastases, mainly by detecting previously unknown extrahepatic disease. FDG-PET is also useful in the follow-up of patients who underwent surgical procedures of the liver, since it is sensitive in detecting residual or relapse malignancy in scarred liver tissue following both resection and local ablative techniques. For follow-up during systemic therapy, early FDG-PET appears predictive for response to therapy.
FDG-PET, Computerized Tomography and Magnetic Resonance Imaging are complimentary techniques in staging and restaging patients with advanced colorectal cancer. A combination of FDG-PET and CT scanning characteristics seems promising, and integrated PET/CT is becoming more widely available, although the exact clinical value and efficacy is not yet fully established. In addition, assessment of these modalities in joint reading sessions with radiologist, nuclear medicine physician, medical and surgical oncologists significantly impacts upon patient management.

**247** INVITED

**Systemic treatment**

H. Schmoll[1]. [1]*Universitätsklinikum Halle, Klinik für Innere Medizin IV, Halle, Germany*

Patients must be divided in 2 different groups: (a) patients with resectable liver metastases and (b) with unresectable liver metastases due to size, number or illeocation (or all of this). For resectable liver metastases (a) standard treatment is perioperative chemotherapy with 3 cycles FOLFOX before and 3 cycles after surgery. This approach is able to significantly prolong the time to recurrence/disease free survival. For the alternative approach which is postoperative adjuvant chemotherapy without preoperative chemotherapy, the data are not consistent. A metaanalysis of 2 trials give some, but not significant evidence in favour of postoperative treatment with either single agent 5FU or 5FU/Irinotecan based combination to prolong disease free survival. However, the level of evidence is stronger for the pre-/postoperative approach and should therefore preferred. However, in patients who had due to some circumstances no preoperative chemotherapy, at least postop treatment should be considered. The role of Bevacizumab (Avastin®) in addition to chemotherapy for postop adjuvant treatment is currently investigated. For group with unresectable liver metastases (b) the treatment of choice is highly active chemotherapy for 4−6 months, followed by surgical attempt to resect all residual disease as much as possible. This approach leeds to a long term survival of 15−25% of the patients depending on the initial situation. The best chemotherapy regimen is at least a triplet based on chemodoublet plus targeted drug or chemotriplet. For kras wild type tumor patients FOLFOX or FOLFIRI plus Cetuximab (Erbitux®) as well as a chemotherapy triplet, eg. FOLFOX/Irinotecan (Campto®) or XELOX/Irinotecan (Campto®) are of some equivalent activity and potentially superior to FOLFOX/Bevacizumab (Avastin®); however, clear data are lacking regarding the value of Bevacizumab (Avastin®) in comparison to Cetuximab (Erbitux®). For kras mutant tumor FOLFOX or FOLFIRI plus Bevacizumab (Avastin®) or FOLFOX plus Irinotecan (Campto®) are the treatment of choice; comparative phase II data indicate that the chemotriplet might be superior in terms of response induction over a Bevacizumab-based chemodoublet. A randomised trial is needed to elucidate the optimal chemotherapy in this situation.

**248** INVITED

**Multidisciplinary perspectives of the management of liver metastases from colorectal cancer (CRCLM)**

G. Poston[1]. [1]*University Hospital Aintree, Oncology, Liverpool, United Kingdom*

We have made major progress over the last 20 years in the management of patients with CRCLM. In 1989, very few patients (mostly those with solitary, easily respectable metachronous tumours) were considered for surgery with curative intent. Most were offered either best supportive care or at

best 5 fluorouracil, with expected median overall survival of 6−8 months. Outcomes could not be more different in 2009.
The definition of surgical resection with curative intent is now the ability to preserve 25−30% of disease-free functioning liver with good vascular inflow and outflow (which accounts for 20% of patients with liver only disease). Five and 10 year overall survival after hepatectomy is 50% and 26%. We now have good evidence to show the survival benefit of ablation therapies over chemotherapy alone in non-resectable disease. Modern chemotherapy regimens combined with state-of-the- art biological therapies can achieve median survival in incurable disease approaching 3 years, and perhaps more significantly can render over 40% of patients with non-resectable liver-only disease amenable to surgery with curative intent. Five year survival for all patients with CRCLM now approaches 30%.
Such progress has only been made possible by the adoption of multi-disciplinary team working (MDT). MDTs are now mandatory by law for the treatment of cancer patients in a number of European countries and being increasingly adopted in the others.

## *Scientific Symposium* (Wed, 23 Sep, 14:45−16:45)
## The management of malignant pleural mesothelioma

**249** INVITED

**Biology of mesothelioma**

P. Zucali[1]. [1]*Istituto Clinico Humanitas, Department of Medical Oncology and Hematology, Rozzano Milano, Italy*

Malignant pleural mesothelioma is an aggressive tumor, with a poor prognosis. Its incidence is increasing worldwide as a result of widespread exposure to asbestos, and is predicted to peak in the next 10−20 years. The results of the available therapeutic resources are poor. Surgery and radiotherapy have a limited role in highly selected patients and systemic therapy is the only potential treatment option for the majority of patients. Despite some definite activity of the novel antifolates such as pemetrexed and raltitrexed, only small steps forward were recently made possible. Pemetrexed and raltitrexed are now a recognized standard treatment. However, the results even in combination with platinating agents, are still meager, with an extension of a median survivals by only 3 months and with a median survival of approximately one year.
An improvement of the knowledge of major molecular pathways involved in malignant mesothelioma is needed in order to define proper targets for the systemic treatment of this disease. Malignant mesothelioma cells show an increased or dysregulated growth. The cells produce and respond to many autocrine growth factors, such as hepatocyte growth factor (HGF), epidermal growth factor (EGF), platelet-derived growth factors (PDGF) A and B, transforming growth factor b (TGFb), and angiogenic factors, such as vascular endothelial growth factor (VEGF). The corresponding receptors to these growth factors activate the PI3K−Akt pathway, which has a crucial role in malignant pleural mesothelioma cell survival and contributes to the anti-apoptotic phenotype. Unfortunately, the clinical results of available target therapeutics are still modest. Several compounds are in pre-clinical evaluation, and interesting results are emerging from cell lines studies. Moreover, novel biomarkers are under evaluation as a useful predictive or prognostic tool. The tailor-made treatment derived from the biologic and genetic characterization of tissue will offer better outcomes against malignant pleural mesothelioma in the future.
The principal goals of this presentation are to summarize the current knowledge in terms of major molecular pathways involved in malignant mesothelioma and outline the therapeutic approaches in development.

**251** INVITED

**Radiotherapy**

C. Faivre-Finn[1]. [1]*The Christie foundation NHS Trust, Department of Clinical Oncology, Manchester, United Kingdom*

Patients with malignant pleural mesothelioma (MPM) often present with advanced symptomatic disease in which thoracic radiotherapy (RT) plays mainly a palliative role. The evidence to support the role of radiotherapy in this disease has mainly been derived from non-randomised data with the exception of the use of prophylactic irradiation to intervention tracts. The impact of radical or palliative thoracic RT on quality of life is not well known. In vitro studies have suggested that MPM is only partially radiosensitive.
**Palliative RT:** is routinely offered to control symptoms such as thoracic pain and dyspnoea on the basis of small retrospective studies. However there is no randomised data demonstrating the impact of palliative RT on symptom control, quality of life or survival.
**Radical RT:** there is no evidence to support the use of radical thoracic RT alone in MPM. This treatment modality is generally not offered as a routine treatment as the dose delivered to the disease is limited by the dose given to the adjacent organs at risk.
**Post operative RT:** the role of surgery for MPM is controversial. The best-documented multimodality approach to MPM is pleuropneumonectomy, followed by chemotherapy and radiotherapy in selected patients with earlier stages of disease. Post operative radical doses to the hemithorax have been reported to be tolerable and seem to decrease the rate of local failure after extrapleural pneumonectomy although no randomised data is available on the impact of postoperative RT compared to surgery alone. Post operative hemithoracic RT without extrapleural pneumonectomy is associated with significant toxicity on the normal lung tissue. Intensity-modulated radiotherapy allows for an increase in dose to the pleural cavity and a reduction in radiation doses to organs at risk. The ESMO 2008 clinical guidelines state that 'Modern radiotherapy techniques allow for delivering high-dose radiotherapy in an attempt to improve local control after EPP'
**Prophylactic irradiation to intervention tracts (PIT):** according to the current literature patients who undergo chest instrumentation, may develop seeding at the site of intervention, leading to subcutaneous tumour in 10 to 50% of cases. This is believed to be reduced by the common practice of prophylactic irradiation to intervention tracts (PIT). However two of the three published randomised controlled trials do not support the use of PIT but the evidence is contentious as these trials were not adequately powered. Furthermore they did not include patients receiving systemic chemotherapy and did not always collect data on the impact of PIT and track recurrence on quality of life and symptom control. The ESMO 2008 clinical guidelines state that 'Prophylactic radiotherapy to reduce the incidence of port metastases is controversial and not routinely applied'.
In conclusion, in MPM there are unmet needs to develop more effective radiation treatments that can improve quality of life and survival. Patients should be offered inclusion in a clinical trial whenever possible.

**252** INVITED

**The role of surgery in the management of malignant pleural mesothelioma**

D. Waller[1]. [1]*Glenfield Hospital, General Thoracic Surgery, Leciester, United Kingdom*

Surgery has a primary role in the diagnosis and staging of malignant pleural mesothelioma (MPM). Therapeutic surgery has a role in symptom control and prolongation of disease-free interval. Radical surgery is intended to remove all macroscopic disease to offer long-term survival as part of multimodality therapy.
Whilst percutaneous biopsy is often used to diagnose MPM thoracoscopy is usually required in early disease. In most cases now medical thoracoscopy is employed but surgical thoracoscopy or open pleural biopsy may be needed in equivocal cases. Staging is as important in MPM as in other cancers particularly as major surgery carries high risk. Mediastinoscopy is the basis of surgical staging and video assisted mediastinoscopy may be combined with video assisted thoracoscopy via the cervical approach to offer diagnosis, staging and pleurodesis at one step.
Symptomatic control of pleural effusion can be achieved by video assisted thoracoscopic surgery (VATS) and talc insufflation. VATS can also be used to perform parietal pleurectomy which controls effusion and retards tumour progression. In cases of entrapped lung VATS may be used to perform visceral pleurectomy to allow lung re-expansion. Dyspnoea cannot be relieved in these cases unless the lung is decorticated.
Complete macroscopic tumour clearance can be attempted in selected patients in order to achieve long-term survival. This is conventionally achieved by extrapleural pneumonectomy (EPP) with en-bloc removal of pleura, lung, pericardium and diaphragm. This operation is associated with high morbidity and an operative mortality of around 5%. There is recently renewed interest in lung-sparing radical surgery or radical pleurectomy/decortication which is best termed total pleurectomy. There is evidence that this approach is equally effective as EPP in more advanced disease and carries lower operative risk and is suitable for a wider population.
Radical surgery alone is not considered optimum treatment and a multi-modality program is preferred. Additional chemotherapy can either be given preoperatively, intraoperatively as intravcavitary therapy or postoperatively. There is debate surrounding all these 3 routes. Additional radical hemithorax irradiation can only be given after EPP and while local disease control can be increased there are potentially toxic side-effects.
As the incidence of MPM increases in Western Europe evidence for these surgical strategies is urgently needed. The paucity of high grade therapeutic evidence is being addressed in anumber of on-going surgical trials. The CRUK sponsored MARS trial has completed its feasibility study of comparing EPP vs no EPP; an EORTC trial assessing the role of post EPP hemithorax irradiation is underway and the MesoVATS trial continues in UK to assess the benefits of VATS pleurectomy/decortication.