

planning and implantation. Currently MR ultrasound fusion is not widely available limiting the application of functional imaging for the LDR technique. HDR Brachytherapy, in contrast delivers radiation dose through after loading catheters with the planning undertaken after implantation. This offers greater flexibility in defining a focal sub volume to be treated, and if CT or MR based planning is used, then image registration of functional imaging sequences taken in the diagnostic setting prior to implantation can be used to accurately define the volume. It is a more flexible system for dosimetry with each catheter contributing to the total dose within a volume, and the dwell time of the source within each catheter defining on a individualised basis each contribution. In contrast LDR brachytherapy uses seeds of a fixed strength and therefore only by altering the density and distribution of seeds can focal therapy or a focal subvolume boost be achieved.

HDR Brachytherapy therefore may offer the greatest opportunity for accurate focal brachytherapy at a technical level. Its main limitation lies in the limited experience as monotherapy and as yet no consensus over the optimal dose fractionation schedule. LDR brachytherapy is supported by a substantial clinical evidence base using a standard prescription of 145 Gy using the TG43 formalism for dosimetry. Thus HDR has technical advantages in flexibility of dose delivery whilst LDR currently has the greater weight of evidence supporting its role and dose delivery as monotherapy.

286 INVITED
Heat, Ice and Light

Abstract not received

Special Session (Mon, 26 Sep, 13:15–14:15) **Advanced Technology for Radiotherapy**

287 INVITED
Clinical Experience With Carbon Ion Radiotherapy

Abstract not received

288 INVITED
Protons for Radiotherapy of Lung Cancer

Abstract not received

289 INVITED
Advanced Photon Therapy

Abstract not received

Special Session (Mon, 26 Sep, 13:15–14:15) **Management of Hilar and Intrahepatic Cholangiocarcinoma**

290 INVITED
Surgical Resection of Hilar and Intrahepatic Cholangiocarcinoma

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Surgical resection remains the only treatment with curative intent for biliary malignancies and this applies in particular to hilar (by definition extrahepatic) and intrahepatic cholangiocarcinoma.

For intrahepatic cholangiocarcinoma, improvement in the efficacy of surgery has, until recently, been limited by the lack of a specific staging system, relative inefficacy of chemotherapy and very limited indication for surgery in case of recurrence. However, since 2010, the AJCC has implemented a specific staging that has been validated and stresses the importance of satellite nodules, vascular invasion and lymph node metastases as the most significant prognostic factors. In particular a pN+ status has a major impact, but requires lymphadenectomy to be performed routinely to be reliable as the prevalence of lymph node metastases is 40% and preoperative imaging is very inaccurate in identifying them. There is very limited data on the benefit of chemotherapy either in the neoadjuvant or adjuvant setting but results from randomized controlled trials performed in non-resected patients suggest that this issue should be addressed. R0 resection is an independent prognostic factor (and should target a margin width of 5 mm at least) as the benefit of an R1 resection (or of resections achieving margins of less than 1 mm) is questionable.

For hilar cholangiocarcinoma, there is also evidence that an R0 resection is mandatory. R1 resections with submucosal tumour cells has a detrimental impact on 5-years survival whereas persistence of superficial tumour cells only impacts 10-years survival. Achieving R0 resections requires a major hepatectomy to be performed and may prove particularly difficult. Mortality rates associated with these procedures is close to 10%. A tailored use of preoperative biliary drainage and portal vein embolisation may reduce this risk. In particular, biliary drainage should be routinely performed before right sided liver resections to reduce the risk of liver failure and surgery should be postponed until serum bilirubin is less than 50–100 µmole/l. It should however be avoided before left-sided resections to reduce the risk of mortality from sepsis.

291 INVITED
Liver Transplantation for Cholangiocarcinoma

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Cholangiocarcinoma has been accepted as an indication for liver transplantation in the beginning of the transplantation era. Due to disappointing long-term results here and in parallel encouraging results in patients with benign disease, cholangiocarcinoma was generally not any more accepted for liver transplantation in recent years. To improve results, more aggressive approaches have been used, the "Abdominal Organ Cluster Transplantation" and the "Extended bile duct resection" (including partial pancreatoduodenectomy), which lead to increased long-term survival rates. However, with improving results after conventional partial hepatectomy, extended procedures in combination with liver transplantation never became a real option in the treatment of cholangiocarcinoma. New awareness for liver transplantation in the treatment of this cancer was raised by patients with hilar cholangiocarcinoma in the context of underlying liver diseases like primary sclerosing cholangitis, precluding liver resection. Current results show increased survival figures, in particular in well selected patients with early tumour stages. Further improvement of the long-term survival may be reached by new adjuvant and neoadjuvant protocols which was successfully introduced into clinical practice by the Mayo Clinic group. Patients with neoadjuvant radiochemotherapy show similar long-term results compared to patients undergoing liver transplantation for other indications. Also photodynamic therapy and the use of new antiproliferative immunosuppressive agents may be an approach for further improvement of the long-term results. Currently, liver transplantation for treatment of cholangiocarcinoma should be restricted to centres with experience in the treatment of this cancer and should be taken into consideration in patients with contraindications to liver resection.

292 INVITED
Adjuvant and Systemic Treatment of Advanced Cholangiocarcinoma

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Surgery with complete tumour resection offers the only chance of long-term survival for patients with hilar and intra-hepatic cholangiocarcinomas. The use of adjuvant therapy varies widely, depending on institutional preference. A number of published case series and retrospective studies exist; however there is only one prospective randomised phase III study available to date (Takada et al, Cancer 2002). In this study, patients with cholangiocarcinomas and cancers of the gallbladder, ampulla or pancreas were randomised to post-op adjuvant mitomycin-C and 5-fluorouracil (5-FU) chemotherapy or surgery alone. An improvement in disease-free survival and 5-year survival was seen only amongst the 112 patients with gallbladder cancer (26% vs. 14.4% respectively, $p=0.0367$) and not in other subgroups. Two ongoing phase III studies will determine the role of capecitabine (NCT00363584) or gemcitabine and oxaliplatin (NCT01313377) versus surgery alone in patients with resected biliary tract cancers.

Unfortunately, most patients present with inoperable or recurrent disease and significant co-morbidity, advanced age, sepsis usually co-exist. A number of phase III studies have demonstrated a survival advantage of chemotherapy over supportive care alone using different regimens including 5-FU, etoposide leucovorin (FELV) (Glimelius et al. Ann Oncol 1996), 5-FU, doxorubicin and mitomycin-C (FAM) (Takada et al. Hepatogastroenterology 1998) and either 5-FU or the gemcitabine/oxaliplatin combination (Dwary et al. J Clin Oncol 2010). In the largest study to date, for patients with a good performance score, the randomised phase III ABC-02 study has established systemic chemotherapy with cisplatin and gemcitabine as a bench-mark for future studies with a median progression-free time of 8 months and median survival of 11.7 months (Valle et al. NEJM 2010), significantly better than gemcitabine monotherapy. Very similar outcomes were observed in a similar Japanese

study (Okusaka et al. Br J Cancer 2010). However, whilst statistically and clinically significant, these gains are modest and these studies serve only as a foundation on which to develop further treatments.

Advanced biliary tract cancer is relatively chemotherapy-sensitive and further chemotherapy studies are underway to expand chemotherapy options.

Attention has also turned to the targeting of cellular pathways pivotal to tumorigenesis including epithelial growth factor receptor (EGFR-), vascular endothelial growth factor (VEGF-) and mitogen-activated protein kinase (MEK-) inhibition, amongst others; no practice-changing phase III studies have yet been reported. Investigators continue to gain a better understanding of the underlying processes in the development and establishment of biliary tract cancers and the effect of targeting one or more of these cellular pathways. Identification of particularly active regimens will also lead to adjuvant and neo-adjuvant studies which are likely to have the greatest impact on patient survival.

Special Session (Mon, 26 Sep, 13:15–14:15) Developments and Management of Lymphoedema

293 INVITED
Lymphoedema: How the Prevalence and Severity of Lymphoedema Related to Cancer has Changed

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This presentation will consider the impact that developments in surgical and imaging techniques are having on the incidence of cancer-related lymphoedema. It will also discuss emerging strategies for early detection of lymphoedema and identification and screening of those most at risk of developing lymphoedema following cancer treatment. These developments have the potential to minimise the severity of lymphoedema and reduce the burden on the patient and the health service.

Finally recent research and developments in the management of lymphoedema with potential to minimise progression and enhance quality of life will be identified.

294 INVITED
Lymphoedema Management Options

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Lymphoedema of the limbs, trunk and genitals is a common side effect following treatment for breast, gynaecological, urological, head and neck and aggressive skin cancers and in sarcomas where radical radiotherapy has been delivered.

For many years treatment for lymphoedema has centred around the 'Four cornerstones' of management namely care of the skin, exercise and positioning, lymphatic drainage and compression either in the form of hosiery of multi layered lymphoedema bandaging; and on a two phase intensive then maintenance programme.

However recent advances have been made in understanding who might be more at risk of lymphoedema together with further treatment options. There is a growing understanding of the role of low level laser therapy, intermittent pneumatic compression devices and early intervention programmes. The role of liposuction for resistant lymphoedema is becoming commonplace where conventional treatments have failed. We have moved on from the Four Cornerstones to be able to offer our patients more choice and autonomy in self management in their own home in line with the survivorship agenda.

This special session will give an overview of the current evidence for all the major therapies used in lymphoedema management.

295 INVITED
The Management of Lymphoedema in Advanced Cancer

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Lymphoedema is a problem commonly experienced by patients with advanced cancer. There are several factors which may contribute to the onset of lymphoedema in these patients including: surgery and radiotherapy, metastatic lymphadenopathy, tumour recurrence, infection or inflammation, reduced mobility and function, effects of medication, hypoalbuminaemia and venous thrombosis.

Symptoms commonly experienced include: swelling of one or more limbs which can extend into the trunk, genitals and head or neck; ulceration;

tension of the affected tissues; heaviness of the limb causing impaired mobility, function and sensation and infection. Up to 67% of patients with advanced cancer experience pain due to oedema and lymphorrhoea (leakage of lymph fluid) can be a further complication.

Cancer patients with lymphoedema can experience a wide range of physical, psychological and social problems which can have a significant impact on their quality of life. A holistic assessment is the first step in understanding the patient's main concerns and priorities with regard to managing their swelling. However, it is important to remember that the burden of treatment on the patient should not exceed the benefit gained and, therefore, treatment will generally have to be adapted and modified to suit patients' individual needs.

This presentation will examine the management of lymphoedema in the patient with advanced cancer.

Special Session (Mon, 26 Sep, 13:15–14:15) Controversies in the Management of Cervical Cancer

296 INVITED
Neoadjuvant Chemotherapy in Locally Advanced Cervical Cancer

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Cervical cancer is the second most common cause of female cancer mortality worldwide. In 1999 the National Cancer Institute (NCI) announcement modified the paradigm of locally advanced cervical cancer (LACC) treatment toward concurrent chemo-radiotherapy, in view of the publication of 5 randomized trials that demonstrated a survival advantage with the addition of cisplatin-based chemotherapy to radiotherapy alone. However, the lack of radiotherapy departments, especially in developing countries, the presumed high incidence of long-term complications and the poor control of metastatic disease have brought about the development of different therapeutic approaches such as neoadjuvant chemotherapy (NACT) followed by surgery.

A meta-analysis of NACT followed by radical hysterectomy showed an absolute improvement of 14% in 5 year survival compared to radiotherapy. Out of more than 800 patients evaluated in this meta-analysis, 441 were from an Italian randomized trial that compared NACT followed by surgery (group 1) with radiotherapy (group 2). Patients with FIGO stage IB2-IIB had 5-years overall and progression free survival significantly longer in group 1. To date, there are not enough data that would support the "best" neoadjuvant chemotherapy regimen. The two randomized phase II studies, SNAP01 and SNAP02, showed that TIP or TEP (epirubicin for adenocarcinoma tumours) provide an average of 42–48% optimal response rate, defined as no residual or residual disease with ≤ 3 mm stromal invasion. In these studies, the achievement of an optimal response rate as above described was the strongest predictor of survival and therefore this endpoint could be considered as a surrogate in trials investigating new therapeutic options. The Cochrane metanalysis indicated that trials using cycle lengths shorter than 14 days or the cisplatin dose greater than 25 mg/m² per week exhibited a greater advantage on the survival of patients with LACC. It indicates that the timing and dose intensity may greatly impact the curative effect of NACT. It seems reasonable therefore to explore dose-dense regimens in this setting.

In conclusion from the data of the literature NACT followed by radical surgery could have an important role in the treatment of LACC, but the appropriate indications and contraindications need to be better identified. Promising results have been already published, but the final answer will be given by the randomized clinical trial carried out by the European Organization for Research in Cancer Therapy (EORTC 55994), which will hopefully demonstrate whether or not NACT followed by surgery will display a better oncological outcome compared to chemo-radiotherapy for IB2-IIB cervical cancer patients.

297 INVITED
Image-guided Adaptive Brachytherapy (IGABT) and External Radiotherapy in Patients With Cervix Cancer

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Concomitant chemoradiation followed by intrauterine brachytherapy (BT) represents the standard of treatment in patients with advanced cervical