of IGF1R monoclonal antibodies was so far focused in patients with sarcoma, and studies are ongoing in children and adolescents evaluating the combination with chemotherapy or mTOR inhibition.

**278** INVITED

**The IGF1 Growth Hormone Axis in Human Development**

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Due to its major roles in initiation, progression and growth of tumours, the insulin-like growth factor (IGF) system, and more specifically the type I IGF receptor, has become a prime target for developing anti-tumour strategies. However, even if inhibiting this signaling pathway appears relevant to block tumour development, it may also affect the multiple physiological functions controlled by these secreted growth factors in particular during childhood and adolescence. In fact, IGFs are key elements that regulate growth and differentiation of many tissues and organs. Their complexity relies in particular on the fact that they are not only expressed in the liver, under the control of the somatotropic hypothalamic-pituitary axis, but also in all tissues where they played major autocrine and paracrine functions. Moreover, the strong homologies between the type I IGF receptor and the insulin one allows the constitution of hybrid receptors that need to be taken into account when developing therapeutic strategies. Studying human pathologies and animal models in which the IGF system is under- or over-regulated can shed lights on the main functions played by these growth factors during human development.

## *Scientific Symposium* (Mon, 26 Sep, 09:00−11:00) **Novel Radiation Technologies and Strategies**

**279** INVITED

**Adaptive Radiation Therapy − Technology and Strategies**

Abstract not received

**280** INVITED

**Integrated MRI-Guided Advanced Radiotherapy**

J.J.W. Lagendijk[1], B.W. Raaymakers[1], M. van Vulpen[1]. [1]*University Medical Center Utrecht, Department of Radiotherapy, Utrecht, The Netherlands*

In Utrecht a radiotherapy accelerator is being developed with MRI functionality. This system offers superb soft-tissue contrast imaging directly from the treatment table. The operator sees the actual beam according to the actual anatomy real time. Due to the dynamic capability of MRI a full inventory of motion, deformation and response can be assessed to minimise the margins for geometrical uncertainties in the tumour position. MRI does not only provide improved target localisation but also better target characterisation by means of functional MRI.
For treatment guidance, MRI can visualise the tumour without the need of surrogates, and can also visualise the surrounding organs at risk. This can be done not only once prior to each fraction but continuously during dose delivery, so also intra-fraction motion, e.g. breathing related motion, can be tracked and corrected for. This presentation will give an overview of the system being developed at the Radiotherapy Department of the UMC Utrecht, the Netherlands in collaboration with Elekta and Philips: a 6 MV accelerator with diagnostic quality 1.5 T MRI functionality. We expect that MRI guided Radiotherapy will become the new standard treatment machine. The moment we see what we do, on line, treatment improvements and dose optimisations are unavoidable. Dynamic on line MRI guidance can produce a breakthrough for difficult tumour sites like the kidney, liver, pancreas, rectum and oesophagus.
The MRI linac systems will be placed in a new Centre for Image guided Oncological Interventions, a close collaboration between Radiotherapy and Radiology. The equipment involved in this new Center and the intended patient categories will be discussed.

**281** INVITED

**Scanned Intensity − Modulated Proton Therapy**

Abstract not received

**282** INVITED

**Laser-Accelerated Proton Therapy**

W. Enghardt[1]. [1]*Technische Universität Dresden, OncoRay, Dresden, Germany*

Considering their interaction with matter beams of protons and light ions should have the potential for increasing the curing rate in radiotherapy. Their physical advantages over conventional therapeutic radiation modalities (ultrahard bremsstrahlung and electrons delivered by medical electron linear accelerators) lead to reduced normal tissue dose and to the possibility of dose escalation within the tumour volume. Additionally light ions show an increased relative biological effectiveness (RBE) at the end of their track, which can be confined to the tumour volume, if an appropriate beam delivery technique (pencil beam scanning) is applied. Up to now these advantages of particle beams could not be translated into improved cure rates for most of tumour species.
For this situation three reasons are relevant: (i) Treatment and quality assurance techniques applied to particle therapy have been adopted from conventional radiation therapy. This is not adequate, since the dose distributions of particle beams are much less robust against minor inaccuracies in the treatment workflow than those of photons. (ii) The number of patients treated worldwide at technological optimal devices in clinical studies of high quality is still low. (iii) The reasons outlined under (i) and (ii) are primarily caused by the high investment and operating costs of particle therapy facilities, which exceed those of conventional facilities by about one order of magnitude.
This situation has led to intensive research on compact acceleration and beam delivery concepts. These include superconducting, dielectric wall and laser driven accelerators. The latter may have the highest potential for miniaturizing particle therapy devices. However, before a clinical prototype will become realistic, several physical, technological and biomedical problems have to be solved requiring intensive research on: (i) high power lasers ($P > 1$ PW) of high repetition frequency ($f > 10$ Hz); (ii) radiator targets, which efficiently convert the laser light into high energy protons ($E > 200$ MeV); (iii) dedicated techniques of dosimetry and quality assurance, which fit to the unusual time structure and pulse dose rate of laser accelerated beams; (iv) comprehensive characterization of the RBE of this novel radiation type via in in-vitro and in-vivo experiments; (v) reduction of the overall size of the irradiation facilities by the combination of laser acceleration and compact beam deliveries.

## *Keynote Lecture* (Mon, 26 Sep, 11:30−12:15) **How Registry Data Has Changed Rectal Cancer Treatment**

**283** INVITED

**How Registry Data Has Changed Rectal Cancer Treatment**

Abstract not received

## *Special Session* (Mon, 26 Sep, 13:15−14:15) **How Should We Treat Good Risk Prostate Cancer − Focally or Entirely?**

**284** INVITED

**Active Surveillance**

Abstract not received

**285** INVITED

**Brachytherapy − High Dose Rate or I-125?**

P.J. Hoskin[1]. [1]*Mount Vernon Hospital, Cancer Centre, Northwood Middlesex, United Kingdom*

Brachytherapy provides the ultimate tool for customising dose distributions within the prostate gland. Low dose rate (LDR) seed brachytherapy with I − 125 or Pd-103 is well established as an effective treatment for good risk prostate cancer with biochemical control rates and survival equivalent to that of the other major modalities of treatment in this setting. Currently high dose rate (HDR) brachytherapy is used to boost higher risk patients enabling dose escalation in that setting and does not have a established role in low risk patients, although there is increasing evidence that HDR monotherapy is an effective treatment with low toxicity in this group of patients.
The convention for both LDR and HDR is to define the clinical target volume by the capsule of the prostate gland and a variable margin encompass potential microscopic extra capsular extension, typically 3−5 mm. Focal treatment requires accurate definition of the dominate lesion or lesions to be ablated. This may be mapped using biopsies or using functional imaging.
Biopsy mapping can be used for LDR brachytherapy transposing the position of the dominant lesion onto the ultrasound images used for

planning and implantation. Currently MR ultrasound fusion is not widely available limiting the application of functional imaging for the LDR technique. HDR Brachytherapy, in constrast 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 Intrahematic Cholangiocarcinoma**

O. Farges[1]. [1]*Hopital Beaujon, Department of Hepatobiliary and Pancreatic Surgery, Paris, France*

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. Ro 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 survivals 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 livr resections to reduce the risk of liver failure and surgery should be postponed untilserum bilirubin is less than 50–100 μmole/l. It should however e avoided before left-sided resections to reduce the risk o mortality from sepsis.

**291** INVITED
**Liver Transplantation for Cholangiocarcinoma**

S. Jonas[1]. [1]*Klinik für Chirurgie, General Visceral and Transplantation Surgery, Leipzig, Germany*

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 antiproliverative 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**

J.W. Valle[1]. [1]*The Christie NHS Foundation Trust, Medical Oncology, Manchester, United Kingdom*

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