intermediate doses of radioactivity are suitable for these relatively slow-growing tumors ("long term low dose, not short term high dose concept"). After each 2 treatment cycles, restaging is performed by morphologic (CT/MRI) and molecular imaging (Ga-68 SST PET/CT), blood chemistry and tumor markers. All data are entered in a prospective structured database (over 250 items per patient). 

NET Center Bad Berka - Results
Retrospective analysis was performed in 1000 patients (age 4 - 85 years) with metastatic and / or progressive NETs, undergoing 1 - 9 cycles of PRRT at our center using Lu-177 (n=331), Y-90 (n=170) or both (n=499). Median total administered activity was 17.5 GBq. Patients were followed up for up to 132 months after the 1st cycle of PRRT. Well-differentiated NETs (G1-G2) accounted for 54 %. Most patients (95.6 %) had undergone at least 1 previous therapy (surgery 86.8 %, medical therapy 55 %, ablative therapy 14.2 % and radiotherapy 3.4 %). The median overall survival (OS) of all patients from the start of PRRT was 52 months (mo). Median OS according to radionuclide used: Y-90 24 mo, Lu-177 55 mo, both (TANDEM or DUO PRRT) 64 mo; according to the grade of tumor: G1 87 mo, G2 55 mo, G3 28 mo, unknown 50 mo; and according to origin of primary tumors: pancreas 45 mo, small intestine 77 mo, unknown primary 55 mo, lung 36 mo. Median progression-free survival for Y-90 alone was 12 mo, compared to 22 mo, for the last therapy cycle was 22 mo, comparable for pancreatic (23 mo) and small intestinal (25 mo) NETs. The use of a combination of Lu-177 and Y-90 takes this heterogeneity into account. Sequential administration of Y-90 and Lu-177 labeled analogues is useful for the treatment of larger tumours and to overcome treatment of smaller metastases respectively in further treatment cycles. Conclusions PRRT lends a significant benefit in progression free survival as well as in overall survival in metastasized and / or progressive G1-2 NETs as compared to other treatment modalities and regardless of previous therapies. Combination of Lu-177 and Y-90 (DUO) based PRRT may be more effective than either radionuclide alone. Up to 10 cycles of PRRT, given over several years were tolerated very well by most patients. Severe renal toxicity can be completely avoided or reduced by nephroprotection applying aminocodins; haematological toxicity is usually mild to moderate (except for MDS which occurs in approx. 3-5% of all patients treated). Quality of life can be significantly improved. PRRT should only be performed at specialized centers as NET patients need highly individualized interdisciplinary treatment and long term care. NETTER-1 is the first Phase III multicentric, randomized, controlled trial evaluating 177Lu-DOTA-Tyr3-Octreotide (Lutathera®) in patients with inoperable, progressive, somatostatin receptor positive midgut NETs. 230 patients with Grade 1-2 metastatic midgut NETs were randomized to receive Lutathera 7.4 GBq every 8 weeks (x4 administrations) versus Octreotide LAR 60 mg every 4-weeks. The primary endpoint was PFS per RECIST 1.1 criteria, with objective tumor assessment performed by an independent reading center every 12 weeks. Secondary objectives included objective response rate, overall survival, toxicity, and health-related quality of life. Enrollment was completed in February 2015, with a target of 230 patients randomized (1:1) in 35 European and 15 sites in the United States. At the time of statistical analysis, the number of centrally confirmed disease progresses or deaths was 23 in the Lutathera group and 67 in the Octreotide LAR 60 mg group. The median PFS was not reached for Lutathera and was 8.4 months with 60 mg Octreotide LAR [95% CI: 5.8-11.0 months], p<0.0001, with a hazard ratio of 0.21 [95% CI: 0.13-0.34]. Within the current evaluable patient dataset for tumor responses (n=201), the number of CR/PR was 18 (18%) in the Lutathera group and 3 (3.0%) in the Octreotide LAR 60 mg group (p=0.0008). Although the OS data are not mature enough for a definitive analysis, the number of deaths was 13 in the Lutathera group and 22 in the Octreotide LAR 60 mg group (p=0.019 at interim analysis) which suggests an improvement in overall survival. The Phase III NETTER-1 trial provides evidence for a clinically meaningful and statistically significant increase in PFS and ORR, and also suggests a survival benefit in patients with advanced midgut NETs treated with Lutathera.
Radiotherapy, e.g. for image guidance and target volume delineation. Compared to rigid registration, deformable image registration (DIR) is much more complex as the number of degrees of freedom in a typical DIR system exceeds the ten-thousands versus 6 for rigid registration. To make DIR tractable, registration systems therefore need to make a compromise between image similarity and smoothness of the deformation, attempting to find the smallest deformation that still optimizes the image similarity. This compromise is achieved by tuning a large amount of parameters, which is the trick of the trade.

DIR is currently considered the most essential and most complicated component of on- and off-line adaptive radiotherapy and its validation is therefore essential. Validation programmes should look at technical, general, and patient-specific performance. Technical and general QA methods include 4D and anatomically realistic phantoms, natural and implanted fiducials, and manually placed landmarks, potentially using mathematical methods to account for observer variation. Visual verification is an essential patient specific form of QA, but an important caveat of deformable image registration is the inadequacy of visual validation to provide a final verdict on the registration accuracy, as completely different deformable registrations can result in the identical images. This is not a problem for descriptive tasks such as Hounsfield unit correction and autocontouring, where organ boundaries are sought, but is highly detrimental for quantitative tasks such as dose accumulation and treatment adaption around tumour boundaries where anatomical correspondence is required. Another unsolved issue is that registration performance is poor around sliding tissues and anatomical changes in the patient and specific care should be taken with clinical decisions that depend on dose summation around such regions. I conclude that QA of deformable registration is complex, and that current algorithms lack biological and biomechanical knowledge. I believe that today it is therefore not safe to use them for dose-accumulation and treatment adaptation around shrinking tumours.

Teaching Lecture: VMAT QA: To do and not to do, those are the questions

SP-0573
VMAT QA: To do and not to do, those are the questions
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Introduction
With the advent of Volumetric Modulated Arc Therapy (VMAT), Quality Assurance (QA) has evolved to a next step regarding complexity. Different parts of the linear accelerator (linac) move synchronously, resulting in a dose delivery that can be highly modulated in both space and time. In this lecture the practical aspects of QA are discussed, in particular focussed on VMAT.

Machine QA
Prior to implementing VMAT treatments in the clinic, the user should be familiar with the dynamic behaviour of the machine. In particular, features such as the lowest maximum leaf speed and the behaviour of the system under both dose rate changes and accelerations/decelerations of the gantry should be determined. Such machine characteristics need to be incorporated in the treatment planning system (TPS) to avoid devising undeliverable plans. To properly measure the dose delivered by the linac, the used measurement systems need to be dosimetrically accurate and have a high degree of spatial and temporal resolution. Usually different QA devices are needed to achieve this.

Patient-specific QA
Before a treatment plan can be delivered clinically, the medical physics expert (MPE) has to be convinced that the correspondence between calculated and measured dose delivery is adequate. This can be achieved by performing patient-specific QA, comparing the measured, integral dose with the computed one in a phantom. For this purpose, a high dosimetric accuracy combined with a high spatial resolution is required. Again, different measurement devices are in general needed to meet these demands. The interpretation of the differences between intended and delivered dose distribution, in terms of a gamma analysis, will be discussed. After gaining experience and confidence with a certain class solution for treatment plans, most MPE resort to using only point dose measurements or computer programs for independent validation. When and how to introduce such alternatives will be discussed in the lecture. The value of continuous patient-specific QA will also be addressed.

Conclusion
After the lecture, the participant should have a clear idea what type of detectors should be used for what purpose and how to optimise patient-specific QA in a busy clinical environment.

Teaching Lecture: Optimising workflow in a radiotherapy department - an introduction to lean thinking

SP-0574
Optimising workflow in a radiotherapy department - an introduction to lean thinking
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Lean Thinking originated from the manufacturing industry in Japan as a method of highly-efficient production. However, Lean Thinking is not confined to manufacturing and as a management strategy focused on improving processes, is applicable to any organisation. It is now well-established in the complex area of healthcare delivery. Lean Thinking has been described as “the dynamic, knowledge driven and customer-focused process through which all people in a defined enterprise work continuously to eliminate waste and create value” (Rebentisch et al, 2004). For a healthcare organisation, it provides a patient-focused, systematic approach to identifying and eliminating waste (i.e. non-value-added activities) through continuous improvement. The key principle of Lean is distinguishing value-added steps from non-value-added steps, and eliminating waste with the aim that eventually every step will add value to the overall process.

The lean philosophy is not intended to reduce the number of employees working in the hospital. It seeks only to eliminate waste in tasks and processes so that time, materials, resources and procedures can be utilised as efficiently as possible with the aim of dedicating more time and effort to patient care without extra cost to the patient or healthcare organisation.

Using case studies and real-life examples, this talk will introduce the lean concepts, principles and tools that contribute to improving efficiency, quality and patient safety in radiotherapy and healthcare.

Symposium: New concepts of tumour radioresistance

SP-0575
Radiotherapy combined with immunotherapy: present status and future perspectives
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Radiotherapy is along with surgery and chemotherapy one of the prime treatment modalities in cancer. It is applied in the primary, neoadjuvant as well as the adjuvant setting. Radiation techniques have rapidly evolved during the past