mathematics, high energy, medical physics and radiation oncology, at the University of Cambridge and Cambridge University Hospitals.
Autosegmentation algorithms were applied for identifying the rectum in prostate radiotherapy (Chan-Vese), and the swallowing OARs (parotids and submandibular glands, pharyngeal constrictors, oral cavity and supraglottic larynx) in H&N radiotherapy (Elastix). CheckTomo, an independent dose calculation system for direct calculation on MVCT images, was integrated into the VoxTox automated processing system. Toxicity data were prospectively collected using electronic case report forms, and all coding to standard scoring systems was externally verified.
For accumulating delivered dose to the rectum, dose surface maps (DSMs) of the rectal wall were generated in order to conserve spatial dose features. Daily delivered DSMs were corrected for positional variations and differences in MVCT field of view, and accumulated. Final accumulated and planned DSMs were parametrised using equivalent uniform dose (EUD) and dose-widths (the lateral extent of an ellipse fitted to a given isodose). Associations with rectal bleeding (RB) at 2 years cumulative incidence were assessed.
For swallowing OARs, the difference between planned and accumulated dose were reported using mean dose. Univariate analyses were performed to assess correlations between baseline clinical factors, mean planned dose, and mean delivered dose, with three toxicity endpoints; xerostomia, salivary duct inflammation, and dysphagia.
Results
For a cohort of 109 prostate cancer patients, accumulated EUD to the rectal wall was systematically lower than planned EUD. Accumulated EUD was the strongest discriminator of RB (AUC 0.682). Spatial features of accumulated DSMs were more strongly associated with RB than those from planned DSMs for dose-widths up to 70 Gy. The accumulated DSM 65 Gy dose-width generated the strongest spatial correlation (AUC 0.664). The same trend was observed from a separate cohort of 140 patients in a subsequent analysis (accumulated EUD AUC = 0.651, 65 Gy dose-width AUC = 0.636). A multivariate NTCP model based on parameters of accumulated dose (incorporating baseline RB and previous pelvic or abdominal surgery) was more predictive of 1 year RB than planned dose (AUC 0.809 v 0.782). Model validation is underway.
Mean delivered dose was higher than mean planned dose for all OARs in a cohort of 141 H&N cancer patients. In addition to confirming previously reported relationships between concomitant systemic therapy and pre-treatment symptoms with toxicity 1 year post-treatment, results also suggest stronger associations with delivered dose than planned dose for all endpoints. For H&N patients receiving Proton Beam Therapy (PBT) this may be particularly important.
Conclusion
The unique VoxTox dataset exploits routine MVCT IGRT scans, already being acquired for the purposes of patient positioning, to calculate motion-inclusive delivered dose to OARs. Results suggest that associations between accumulated dose and toxicity are stronger than those from planned dose, and this has been verified in a separate cohort in the case of the rectum. Information on spatial dose features may reveal intra-organ radiosensitivities, which could be useful when identifying patients on treatment who would benefit from adaptive radiotherapy, and may also be relevant for patients receiving PBT.

Poster Viewing: Poster viewing 1: Breast and Skin

PV-0041 Randomized therapeutic trial of combined pentoclo versus placebo in radiation-induced plexopathy
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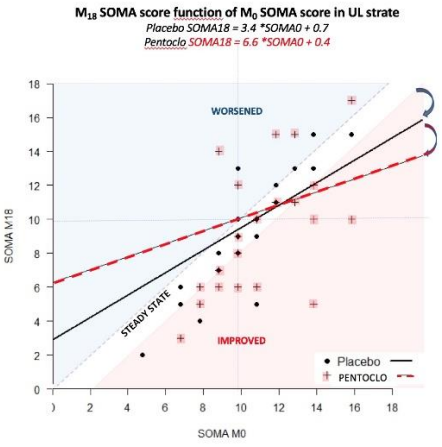
Purpose or Objective
Radiation-induced plexopathy(RIP) is a rare and severe peripheral nerve complication after RT for cancer, without any existing treatment that stabilize or slow down neurological progression. Preclinical and clinical studies showed that combined pentoxifylline-vitamin Etreatment(PENTO) significantly reduced radiation-induced fibrosis, and that the combination with clodronate (PENTOCLO) allowed healing of progressive mandible osteoradionecrosis and a reduction of some neurological symptoms.
Material and Methods
We conducted a randomized, placebo-controlled, double-blind, monocentric trial in RIP patients. Subjects were screened among adults referred to Hôpital Saint-Louis, for limb RIP, after irradiation including axillar-subclavian (breast, lung) or lumbar-iliac lymph area (Hodgkin, seminoma, uterus), excluding recurrence with MRI and PETscan. Included patients were randomized for a daily oral 18 months treatment, in two arms, PENTOCLO (Pentoxifylline 800mg,Tocopherol 1000mg, Clodronate 1600 mg 5d/7) or triple PLACEBO.
Primary outcome measure at M_{18} was the SOMA score quoting neurological symptoms divided in 3 domains: pain, paresthesia and motor disability. Secondary endpoints were sensitivity measures (pain - paresthesia VAS), motor function (ODSS, muscle testing), neurological examination, nine hole peg test/ timed 25-foot walk), quality of life (SF36, CGIC/PGIC); and electromyography.
Results
Between 2011/03 and 2016/10, 59 patients were included (1 false inclusion developing neoplastic plexopathy): 29 in the placebo (P) group vs 29 in the active (A) group. 46 patients had upper limb RIP (mean 68y) and 12 lower limb RIP (59y), irradiated 26 ±8y before, with neurological symptoms for 5 ± 5y. SOMA at $M_0$was 9 (0-6-3 for each domain) in P vs 9 (1-6-3) in A, with severity bias in A group disfavor.
At M_{18}, 51 patients (25 P vs 26 A) were analyzed (7 early discontinuations).No significant difference was observed at M_{18}between P and A groups on the primary outcome: global SOMA 8.7 vs 8.8 (p 0.81) with a probable lack of sensitivity of our score.Secondary outcomes showed, in UL strate (figure), a trend for improvement of pain and paresthesia in A group, as assessed by the SOMA score subdomain for pain (1.22 in P vs 0.87 in A) and VAS paresthesia (4.4 in P vs 3.4 in A).
Adverse events were detected in 81% patients, but no difference was observed between the two groups. There was an unexpected excess of RI complications (30%) in both groups, while expected vascular and digestive complications were more frequent in A (+9%).
RIP natural history was lightened by an excess of vascular stenosis in UL stratum (60%), threatening in third, representing an unexpected neurological severity bias.



Conclusion
This was the first randomized pharmacological drug trial in RIP. No significant therapeutic effect of PENTOCLO was detected. There is a need to develop more sensitive measures to detect the effect of investigational drugs in RIP.

PV-0042 Radiation related lymphopenia as a predictor of locoregional recurrence in early breast cancer
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Purpose or Objective
Many studies reported that radiation related lymphopenia (RRL) was associated with treatment outcome in various cancers. However association between RRL and treatment outcome in early breast cancer (EBC) was rarely studied. This study aimed to investigate whether RRL could predict clinical outcome in EBC patients.
Material and Methods
We analyzed 216 EBC patients (stage IA-IIB) treated with adjuvant radiotherapy (RT) after partial mastectomy from 2004 to 2012 in our institution using Kaplan-Meier plots and the Cox proportional hazards model. All patients did not receive chemotherapy. Peripheral absolute lymphocyte counts (ALCs) during two years after RT were collected from each patient. They were divided into pretreatment ALC (ALC0), ALC 3-5 months (ALC1), ALC 9-11 months (ALC2), ALC 15-17 months (ALC3), and ALC 21-23 months (ALC4) after RT.
Results
ALCs after RT had a tendency of slow increase after rapid decline (median [range] ALC0 1847 cells/μL [623-4085], ALC1 1479 cells/μL [437-3500], ALC2 1626 cells/μL [775-3193], ALC3 1730 cells/μL [854-4408], and ALC4 1855 cells/μL [899-3793]). The 86 patients with ALC1≤1400 cells/μL had significantly lower 8 years locoregional control rate than 118 patients with ALC1>1400 cells/μL (80.5% vs. 98.3%, *P*=0.012) while there was no difference in 8 years disease specific survival rate between two groups (98% vs. 97.1%, *P*=0.758). Young age (≤40 years), lymphopenia (ALC1≤1400 cells/μL), and high histologic grade were significant predictors of locoregional recurrence (LRR) in multivariate analysis (hazard ratio [97% confidence interval] 1.39 [1.18-13.7] *P*=0.026, 1.74 [1.21-26.8] *P*=0.028, and 2.3 [2.6-38.4] *P*<0.001).
Conclusion
Low ALCs 3-5 months after RT were associated with LRR in EBC patients. Therefore RRL could be a potential predictor for LRR of EBC.

PV-0043 ESTRO guidelines for volume delineation for RT after immediate implant-based reconstruction
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Purpose or Objective
on behalf of the ESTRO Working Group on Breast reconstruction and radiation therapy: a contouring project.
Immediate breast reconstruction is increasingly used after mastectomy, even if radiation therapy (RT) is indicated. Contouring guidelines in case of postmastectomy RT (PMRT) after implant-based immediate breast reconstruction are missing (IBR-i). We developed delineation guidelines based on a consensus between a global group of breast cancer experts.
Material and Methods
After designing the project by the core group ,an invitation letter was sent to an international multidisciplinary group of experts (including breast surgeons, radiation oncologists, and clinical oncologists) inviting them to participate in the consensus guidelines. The project included: a web-questionnaire, contouring exercise, group discussions, and literature review.
Results
Based on mailings, the first contouring round, video conferences and a plenary discussion, guidelines are drafted to be validated in the prospective Danish DBCG RT Recon Trial randomising early breast cancer patients between immediate versus delayed breast reconstruction after mastectomy followed by loco-regional RT. Approximately 5-10% glandular tissue is retained after conventional total mastectomy, and more in cases of skin/nipple sparing mastectomy. Therefore, our recommendations include performing a careful evaluation of the patient using visualization/palpation, planning CT, and the extent of the contralateral breast (if intact), to determine the *cranio-caudal borders* of the CTV. The CTV includes the "residual breast tissue and the (subcutaneous) draining lymphatics", thereby excluding the implant. The location of the residual glandular tissue varies; in most cases it is found laterally in the breast, mainly in the “axillary-tail”. We recommend consulting with the breast surgeon about the anatomical borders of the breast-skin. Moreover, in cases of a muscle flap/implant procedure, the transplanted flap including its overlaying skin is not part of the target volume, for which the scars should be marked for proper delineation.
The implant and the contralateral breast should be delineated on planning CT as well as all other organs at risk for treatment planning
purposes.
Table 1: ESTRO delineation guidelines for the CTV in case of implant-based immediate breast reconstruction
Figure 1: Retro-pectoral implant. The CTV is delineated in pink.
Conclusion
The use of target volume guidelines in the setting of IBR-i, based on recognised zones of tumour recurrence risk, aims to reduce inter- and intra-observer variation. They should be reserved for cases for which the disease staging (mainly T-stage) and surgical procedures used are well-defined. These guidelines are being validated in the DBCG reconstruction trial.

PV-0044 Mastectomy or breast-conserving therapy for early breast cancer: outcome comparison of 7565 cases
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