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Session A – Oral presentations breast

Multicenter Phase II study of Intraoperative radiation therapy in early breast cancer in Japan

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Background: For early breast cancer, breast-conserving surgery and whole breast irradiation 50 Gy (± boost) for remaining breast is the standard treatment. However, because whole breast irradiation costs 5 weeks outpatient treatments, we need to develop new method to shorten the period of irradiation in Japan. Intraoperative irradiation therapy (IORT) for the remain mammary grand (21 Gy/fr), one of the accelerated partial breast irradiation (APBI) methods, with properly case selection was reported to have equal ipsilateral breast tumor recurrence (IBTR) rate comparing with the conventional whole breast irradiation by phase III trial (Veronesi U, Lancet Oncol 2013, Vaidya JS, Lancet 2014, Stmad V, Lancet 2016). This procedure is positioned in suitable group by ASTRO guideline 2017. We performed multicenter phase II study of IORT in early breast cancer (UMIN00003578), because we have no data for Japanese breast cancer patients with IORT. **Purpose:** To investigate the efficacy and safety of IORT. **Patients and methods:** Eligibility criteria: 1) T < 2.5 cm, 2) to have hope for breast conserving surgery, 3) ≥ 50 years old, 4) surgical margin >1cm, 5) intraoperative pathologically free margins, 6) sentinel node negative and 7) written informed consent. Exclusion criteria: 1) contraindications to radiation, 2) past radiation therapy for the same breast or chest, 3) extensive intraductal component, 4) a tumor located in the axillary tail of the breast. Procedures: 1) sentinel lymph node biopsy, proven to node negative, 2) Partial resection with at least 1cm margin, 3) microscopic assessment of margins by frozen sections, 4) to protect the chest wall, install the lead disk between the grand and major pectoralis muscle, 5) suture of the remaining breast, 6) irradiation of 21 Gy (90% dose), used by MOBETRON® (IntraOp Medical Corporation) or Clinac® 21EX (Varian Medical Systems, Inc.). Primary endpoint: IBTR rate. Secondary endpoint: safety (or toxicity). Toxicity was evaluated with the Common Terminology Criteria for Adverse Events (CTCAE) V4.0. Target number of subjects: 140 cases. **Results:** From April 2010 to April 2015, 142 patients were enrolled and accrual was completed. 129 patients underwent IORT at 21Gy. Median follow up time is 51.5 months (range 30.0-89.0). Stage 0; n=4(3.1%), Stage I; n=98(76.0%), Stage IIA; n=27(20.9%). The intrinsic subtypes of patients were followed, Luminal type; n=116(89.9%), Triple Negative; n=9(7.0%), HER 2; n=4(3.1%). IBTR occurred in 4 cases (3.1%, [95%CI: 0.9-0.78]). Adverse events were, deep connective tissue fibrosis G1: 78.1%, postoperative hemorrhage G 1: 4.7%, wound infection G 3: 1.6%, G 2: 1.6%, G1: 1.6%, soft tissue necrosis G 3: 0.8%, G 2: 0.8%, G1: 1.6%, wound dehiscence G 1: 2.3% and pain G 1: 8.6%.**Conclusion:** IBTR was low in patients with IORT at 21Gy, and this treatment was tolerated well in Japanese women as well as conventional breast irradiation.

The implementation of INTRABEAM at our Hospital

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Objectives: Radiation therapy has an important role in treating the early stage of breast cancer after a conserving surgery to improve relapse free survival. The recurrences after surgery trend to occur preferentially at tumour bed site. Partial accelerated irradiationand intraoperative radiation treatment (INTRABEAM®) of the breast are strategic accomplishments focused on the surgical bed.

This study has two main purposes: to assess the acute toxicity with INTRABEAM® and to determine the patients who benefit of INTRABEAM® as exclusive radiotherapy treatment. **Material and methods:** Since December 17, 2014 until January 25, 2017 a retrospective study was conducted on a total of 85 women diagnosed with early stage of breast cancer treated with lumpectomy. All of them were suitable to receive at the surgical act a single fraction of irradiation with INTRABEAM®. **Results:** The acute toxicity was low, with no grade III erythema. The most frequently found were seroma in 26 patients (30.5%) which only 1 required drainage, and hematoma in 9women (9.4 %). INTRABEAM® as an exclusive radiotherapy treatment could be performed in 30% of patients. The remaining 70% was treated as a boost. The applicator device most used measured 3.5 cm and the average irradiation time was 20.83 minutes. **Conclusions:** INTRABEAM® is an increasingly common approach in the treatment of early-stage breast cancer and we would like to demonstrate our experience in the Catalan Institute of Oncology. It presents important advantages over conventional radiotherapy maintaining the tumour control, improving less toxicity and shortened treatment courses too.

The effect of accelerated partial breast irradiation using intraoperative and external beam radiotherapy on quality of life of breast cancer patients.

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Purpose: To investigate health related quality of life (HRQL) in older breast cancer patients after two types of Accelerated Partial Breast irradiation: intraoperative radiotherapy (IORT) and external beam APBI (EB-APBI). **Material and methods:** Between 2011 and 2016 women ≥60 years with breast tumours of ≤30 mm undergoing breast conserving therapy were included in a prospective multi-centre cohort study. Patients were treated with electron IORT (1x23.3 Gy prescribed at 100%) (n=268) or photon EB-APBI (10x3.85 Gy daily approximately 4 weeks after surgery) (n=207). All patients received EORTC QLQ C30 and BR23 questionnaires before surgery and at several time points up till 1 year, and were eligible for this analysis if a baseline and at least one of the follow up questionnaires were available. A linear mixed model was used to analyse all HRQL subscales across the first year after treatment between groups, with time points baseline, 3, 6 and 12 months. Additionally, EORTC scales were compared cross-sectional post-operative, at 3 months (short term) and at 1 year (long term). Treatment effect and predictors for global health status (GHS) at 1 year were analysed using multivariable analysis. A p-value of ≤0.01 was deemed significant for repeated measures and multiple testing. For EORTC scales, differences of ≥10 points between groups were considered clinically relevant. **Results:** For this HRQL analysis 203 IORT and 157 EB-APBI patients were eligible. Compliance was 94% at 1 year. Linear mixed model analyses demonstrated that emotional functioning and future perspective were significantly worse in IORT treated patients. However both scales improved significantly during follow up in both groups and there were no clinically relevant differences between groups. No significant difference between groups was observed for all other scales. Furthermore, for all other scales there was a tendency to temporarily worsen after treatment and steadily improve up until 1 year without clinically relevant differences between groups. Cross-sectional analysis showed that postoperative fatigue and role functioning were significantly worse in IORT patients, but the difference was not clinically relevant. Both at 3 months and at 1 year after treatment none of the functioning or symptom scales were significantly different between the treatment groups. Multivariable analysis of GHS at 1 year identified comorbidity (OR -8.1; -13.9 - -2.4) and systemic treatment (hormonal and chemotherapy) (OR -12.5; -20.1 - -4.8) as significant predictors of GHS. **Conclusion:** EB-APBI and IORT were well tolerated. Despite worsening at 3 months after treatment, HRQL improved thereafter and was back to normal at 1 year after treatment in both groups. Treatment with hormonal and chemotherapy and comorbidity seem to be risk factors for worse GHS at one year.NB: This data will also be presented at the ESTRO 2018 conference.

Acute toxicity after intraoperative electron radiotherapy (IOERT) followed by whole breast irradiation for early stage breast cancer - a retrospective analysis of 134 cases

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Purpose: Retrospective evaluation of toxicity and local recurrence rate after intraoperative electron radiotherapy (IOERT) followed by whole breast radiotherapy in patients with early stage breast cancer. **Methods:** 134 patients treated between 11/2014 and 12/2017 with IOERT followed by percutaneous radiotherapy of the whole breast were analyzed. IOERT was applied as boost radiotherapy according to the current German Breast cancer guidelines. Patient, tumor and treatment characteristics as well as clinical outcome and toxicities were evaluated. IOERT was administered directly after lumpectomy using a dedicated mobile accelerator (Mobetron, INTRAOP). High-energy electron (6–12 MeV) beam radiotherapy was applied with a total dose of 10 Gy (prescribed to the 90% isodose). **Results:** 134 female patients (median age 57 years (range 29-74 years)) with early stage breast cancer were evaluated (46.3% right sided, 53.7% left sided). Preoperative staging was cT1 (9.0%), cT1b (11.9%), cT1c (42.5%), cT2 (33.6%), cN0 (88.8%), cN+ (8.2%), cNX (3.0%) and grading was G1 (32.8%), G2 (45.5%) and G3 (16.4%). Molecular subtypes were luminal A (76.9%), luminal B (12.7%), HER2-phenotype (4.5%) and triple negative breast cancer (6.0%). 21.6% of the patients received neoadjuvant chemotherapy before resection. Whole breast radiotherapy, following resection was applied as percutaneous radiotherapy with a median total dose of 50 Gy (range 40.05-50.4 Gy) in either normofractionated single doses (1.8-2.0 Gy) or hypofractionaed single doses (2.67 Gy). Median follow up was 14 months (range 1-45 months). During follow up, 0.9% of the patients developed an isolated local recurrence, 5.6% of the patients suffered from isolated distant metastasis and 0.9% from simultaneous local recurrence and distant metastasis. Grade 2 or higher toxicity (wound infection, seroma, wound dehiscence, hematoma) according to CTCAE v3.0 was seen in 10.4% of patients, grade 3 toxicity was seen in 0.8% of patients. There were no grade 4 complications documented. **Conclusions:** Acute toxicity after IOERT is acceptable and comparable with current publications. Longer follow up will be required for clinical outcome data.

Targeted intraoperative radiotherapy for breast cancer the experience of institut Imor

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Purpose: To evaluate our experience with Targeted Intraoperative Radiotherapy as a boost followed by whole breast irradiation and in selected patients, as Partial Breast irradiation technique. **Material and methods:** 160 patients between 34 and 92 years old with breast cancer were included. Targeted Intraoperative Radiotherapy (TARGIT) was performed, between January 2014 and March 2018,immediately after Breast Conserving Surgery (Lumpectomy and Sentinel Node biopsy and Linfadenectomy if positive sentinel node), using the mobile X-ray system Intrabeam™ wich produces low-energy photons (30- 50 KVp) with a steep dose fall-off in soft-tissue delivering 20 Gy at a radius of 1 mm from the surface, an average of 5 Gy at 10 mm and 1 Gy at 27 mm in about 20 minutes with an spherical applicator of different diameters depending on the size of the lumpectomy cavity. Despite the steep gradient in physical dose, an effective uniform biological dose is distributed inside a rim of about 10 mm around. The EBRT was performed on a LINAC, with conventional fractionation (50Gy in 25 fractions); and hypofractionation (40,05 in 15 fractions, 40,5 in 15 fractions or 42,6Gy in 16 fractions). **Results:** The clinical stages included: Node Negative: cT1 Breast Cancer, 103 patients (64,38%) cT2 32 patients (20%); cT3 2 patients (1,25%) and cTis 7 patients(4,38%). 16 patients had node involment (pN1a) (10%): 5 T2N1 and 2 T1cN1. Pathological findings : Infiltrating ductal carcinoma, 129 patients(80,62%); infiltrating lobular carcinoma, 14 patients(8,75%); metaplasic , 2 patients (1,25%); DCIS, 5 patients (3,13%) other histologies 10 patients (6,25%). IHC findings: Luminal A, 56 patients(35%); Luminal B Her2Neu negative, 64 patients(40%); Luminal B Her2 Neu positive, 17 patient(10,63%); HER2 NEU type, 6 patients(3,75%) and Triple negative, 12 patients(7,5%) the remaining five patients are CDIS (3,13%). 60 patients underwent neoadyuvant

chemotherapy with complete pathological response in 27 cases and partial response in 33 cases. 54 patients underwent oncoplastic surgery before IORT. 20 Gy were applicated to the surface of spherical applicators between 20 and 50 mm. placed in the surgical bed in an average time of 24 minutes (range 11 to 45 minutes). 42 patients between 52 and 92 years(26,25%), with early breast cancer, favorable molecular type, underwent intraoperative radiotherapy (IORT) alone. 115 patients underwent TARGIT +EBRT: 86(53,75%) underwent IORT plus whole breast irradiation , 9(5,63%) IORT plus whole breast irradiation with SC and level III axillary areas, and 20(12,5%) IORT plus WBI with SC and I-III axillary nodal areas. Seroma was diagnosticated by US in 71 patients, in clinical examination, 21patients, fat necrosis was found in 4 patients. Cosmetic result was excellent and good in 97 patients followed until June 2017. Only 1 contralateral recurrence was found in 4 years. **Conclusions:** Targeted Intraoperative Radiotherapy with intrabeam is an easy procedure that allows an optimal localization of surgical bed with minimum increase in surgical time. The APBI with Intrabeam™ is feasible in selected patients however a long term follow up is needed.

Eliot-boost phase II clinical trial for breast cancer: Preliminary results from a single center

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PURPOSE: To report preliminary results of a single center phase II clinical trial aimed to analyzed the outcome and main toxicity in patients affected by breast cancer (BC) undergoing conservative surgery and electron intraoperative radiation (ELIOT) boost, followed by hypofractionated external beam radiotherapy (EBRT). **MATERIALS AND METHODS:** From February 2012 to March 2017, 92 early BC patients underwent conservative surgery and ELIOT boost, followed by EBRT at Papa Giovanni XXIII Hospital in Bergamo (Italy). Patients inclusion trial criteria were: infiltrating carcinoma histology (T1-2, N0-1, M0), unifocality or bifocality (maximum distance between two lesions ≤ 2 cm), PS (ECOG) ≤ 2, age > 18, premenopausal status. ELIOT boost was delivered for all patients at the level of tumour bed by a dedicated linear accelerator NOVAC 7 HITESYS (NRT, Italy), using 9 MeV electron beam, a single dose of 12 Gy at 90%. EBRT was given at the whole breast in 13 daily fractions of 2.85 Gy. Acute and late toxicity were assessed using RTOG toxicity scale. **RESULTS:** Fifty-two patients (56.5%) started EBRT boost in 28 days after ELIOT boost procedure.Current median follow up was 24 months and is too short to evaluate local control. After ELIOT, 2 patients underwent mastectomy, after the identification of another breast metachronous nodule and BRCA1 mutation respectively. Four patients underwent conventional scheduled EBRT: 3 for the presence of unfavourable prognostic disease factors as discovered on the surgical specimen and 1 for severe post-surgical side effects. Most patients had slight local post-surgical oedema: 1 patient had necrosis of the scar area. After EBRT, slight skin erythema (G1) was evidenced in all patients. Considering late toxicity, slight scar fibrosis (G1) was assessed in most patients: 1 patient showed scar retraction and 1 dehiscence of surgical scar. **CONLCUSION:** The advantages of the ELIOT-boost followed by hypofractionated EBRT in early BC are the reduction of treatment duration, the delineation of tumor bed under direct visual and palpable evaluation, no adjuvant chemotherapy delay and the immediate inhibition of cells repopulation. With these preliminary results, it seems to be manageable with acceptable acute toxicity. A longer follow up is needed in order to evaluate local control and late effects rate.

Intraoperative electron (IOERT) boost as current clinical practice in breast cancer patients: The Italian multicentric experience

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Purpose and Objective: The effect of a radiation boost on the risk area in the treatment of early stage breast cancer has been investigated in many studies. The intraoperative radiotherapy electron boost (IOERT) allows higher doses in the tumour bed and many experiences reported an incidence of local recurrence near zero. The most of Italian Centres in which IORT is executed as boost assumed this practice as current clinical one. A joint analysis of data was performed about all patients treated with IORT boost, to investigate the role of the technique on local control, survival, aesthetic valuation and toxicity and contribute to homogenize treatment modalities. **Materials and Methods:** Ten Italian Institutions participated in HIOB study, the multicentre European trial in which IOERT boost of 10 Gy is combined with hypofractionated WBI (2.7 Gy x 15) for stage I/II breast cancer. All HIOB patients were stratified for age groups. From June 2016 patients older than 50 were excluded from HIOB statistical analysis and, when IOERT boost was established as a standard of care, the treatment has been performed anyway. Furthermore, many patients who did not have HIOB inclusion criteria were treated with IORT boost outside the protocol. All these patients were examined. The valuation of acute and late toxicity was performed using WHO scale and the aesthetic result was assessed. **Results:** From January 2011 to March 2018, in seven Italian IOERT Centres, a total of 800 patients (age range 29-75), I° and II° stage breast cancer and ECOG performance status < 2, were treated with an anticipated boost dose of 9-12 Gy to PTV (tumour volume with a radial margin of 1 to 2 centimetres). The boost was delivered with movable Linacs. All the patients received additional whole breast irradiation (WBI), with conventional fractionation or hypofractionation. The median follow-up was 52,7 months (range 3-84). Seven local recurrences were observed (0,87%). Only 2 of them were “in field” true recurrences (0,25%). Perioperatively, no major complications were observed. G1-G2 acute toxicity occurred in 32 patients (4%) and no late complications associated with IOERT were observed. Cosmetic result was very good and even better than patients treated with external beam boost (0% telangiectasias, 13% asymmetry of the breast profile). The overall DFS was 97,3%, 5 patients developed distant metastasis and 1 died of disease. **Conclusion:** Our data suggest that IOERT as anticipated boost during breast-conserving surgery is a reliable alternative to conventional postoperative fractionated boost, even in medium-long term follow up. Further research is required to clarify several issues such as identification of the most appropriate subgroups of patients for IOERT boost or the best fractionation of postoperative radiotherapy. In the examined Italian Centres anticipated boost with electrons (IOERT) was established as a standard of care.

Targeted intraoperative radiotherapy (TARGIT IORT) during breast conserving surgery for early breast cancer in patient after breast augmentation with implants

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Background: Targeted intraoperative radiotherapy (TARGIT) has become a standard option during breast conserving surgery for selected cases of early breast cancer and over 20,000 patients have been treated in over 300 centres around the world. Although a growing number of patients are presenting with implants after breast augmentation, no data have been published yet regarding the safety of TARGIT with implants in situ. TARGIT IORT as a replacement of whole breast irradiation is an important issue in this context because of the high rates of capsular fibrosis following EBRT in such patients. **Methods:** We are reporting the outcome of a cohort of 11 patients from 5 centers, who received TARGIT during breast conserving surgery for early breast cancer, had undergone breast

augmentation with implants before and wanted their implants to stay in situ. Patients were informed that no published data existed and decided for this approach on an individual basis. 3 patients received additional EBRT after TARGIT IORT because of presence of EIC or LVI.TARGIT IORT was performed using Intrabeam - 50 kV – X-rays delivering 20 Gy prescribed at the surface of the tumor bed during the initial lumpectomy procedure. **Results:** Follow-up varied from 76 months to 9 months. 10 patients presented with invasive breast cancer, 1 patient with DCIS. There were no procedure related complications. No breast cancer-related events or any events in any of the patients occurred to date and none have needed to have change of implant. **Conclusion:** This series of patients with TARGIT during breast conserving surgery for early breast cancer after breast augmentation with implants in situ revealed no safety concerns. Although limited by the small number of cases our results give some confidence in discussing this option with suitable patients. To expand this series, we are gathering details about other cases from the whole TARGIT group worldwide.

Targeted Intraoperative Radiotherapy for the Management of Ductal Carcinoma In-Situ of the breast

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Background: Multiple randomized and non-randomized trials have demonstrated the efficacy of targeted intraoperative radiotherapy (TARGIT) in the management of early stage invasive breast cancer treated with breast conserving surgery (BCS). In the present analysis, we evaluate the efficacy of TARGIT and BCS surgery in the management of ductal carcinoma in situ (DCIS). **Methods:** Between November 2007 and December 2017, 54 women with a preoperative diagnosis of DCIS underwent bilateral digital mammography and bilateral breast CE-MRI prior to BCS and TARGIT. Patients were considered eligible for TARGIT based on a preoperative tissue diagnosis of DCIS, lesion size ≤4cm in maximal diameter on both digital mammography and CE-MRI, and resectability with clear surgical margins using BCS. Post-operatively, the DCIS lesion size determined by imaging was compared with lesion size and surgical margin status obtained from the surgical pathology specimen. Local recurrence was assessed in patients successfully completing breast conserving therapy. **Results:** Fifty-nine (59) patients completed BCS and TARGIT. Five of these patients were upstaged to invasive breast cancer on final surgical pathology and subsequently underwent sentinel node biopsy, yielding 54 patients with pure DCIS evaluable for the efficacy endpoint. Mean patient age was 58 years (range 42-83) and mean lesion size was 14.2 mm (2.2-39) by imaging and 14.5 mm (2-51) by surgical pathology. Forty-nine (49) of 54 patients met criteria for negative margins (i.e., margins ≥2 mm). Two of the five patients with positive margins underwent mastectomy due to extensive imaging-occult DCIS. The remaining 3 patients underwent successful re-excision at a subsequent operation followed by whole breast irradiation (WBI) per protocol, yielding 52 patients that BCT of which 49 received BCS with TARGIT but no WBI. Among these patients, four (4) local recurrences were observed at a median follow-up 42 months (0-116) yielding a local recurrence rate of 8.2% (4/49). Only one of the 4 recurrences were invasive. Two of the patients with local recurrence received TARGIT at the time of a second operation (post-pathology), resulting in a local recurrence rate of 4.3% (2/47) among women receiving TARGIT at the time of initial BCS (pre-pathology). **Conclusion:** TARGIT is a reasonable radiotherapy option for selected women with DCIS managed with BCS. The risk of local recurrence may be reduced by restricting the timing of TARGIT delivery to women receiving intraoperative radiation at the time of initial DCIS resection.

Long-term outcome of DCIS of the breast treated with intraoperative radiotherapy with electrons: experience of the European Institute of Oncology

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Purpose and background: to investigate the local outcome of patients affected by ductal carcinoma in situ (DCIS) treated with breast conservative surgery and partial breast irradiation (PBI) with intraoperative electrons (IOERT). DCIS has recently been included in the suitable category according to ASTRO guidelines on PBI, mainly on the basis of reports using MammoSite. So far, no data have been published regarding the use of IOERT in DCIS. **Material and Methods:** From 1998 to 2010, more than 1450 patients with DCIS were operated on at the European Institute of Milan. Out of them, 179 were treated with IOERT as the sole adjuvant radiotherapy. Indication for IOERT was given on the basis of vacuum-assisted core biopsy and radiological extent of microcalcifications ≤ 2 cm. The treatment schedule consisted of 21 Gy at 100% isodose, immediately after the removal of the lesion with conservative surgery. Hormonal therapy was offered at the discretion of clinicians, according to patients' preference. **Results:** At the time of writing, clinical and pathological data were available on 161 patients, with a median age of 55 years (range 29-80 years). The median pathological size of DCIS was 1.5 cm (0.2-5-6 cm). Necrosis was present in 62% of the cases and multifocality was detected in 10% of specimens. Regarding grade, 30% of DCIS were grade 3. At 2 years, there were 16 events, resulting in a cumulative incidence of local recurrence of 9.9%. In detail, 5 (31%) were in situ and 11 (69%) were invasive recurrences. As the length of the follow-up increased, the cumulative incidence of local failure raised to 18% at 5 years and to 24% at 8 years. At the last follow-up, in situ and invasive events accounted for 37% and 63% of local relapses, respectively. Analyses regarding clinical, pathologic, and treatment-related variables (such as tumor grade, necrosis, receptor status, KI-67, cerbB2 status, receptor status, margins of excision, and the use of adjuvant hormonal therapy, size of IOERT collimator, histological subtypes) associated with the development of local recurrence are being performed. **Conclusion:** Partial breast irradiation using intraoperative electrons should be considered with caution in DCIS. Ongoing subset analyses will help to identify selected DCIS for which IOERT might be a reasonable option.

Intraoperative radiotherapy in post-neoadjuvant chemotherapy breast conserving surgery in triple negative and her-2 positive patients at Instituto Nacional de Enfermedades Neoplásicas from 2014 to 2016

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Objective: To describe the results of intraoperative radiotherapy (IORT) using a 50 kV X-ray source versus teletherapy to the operative bed in HER2 and Triple Negative (TN) patients with post-neoadjuvant conserving surgery. **Methods:** HER2 and TN breast cancer cases were reviewed, which underwent conserving surgery after neoadjuvant chemotherapy and received IORT or teletherapy to the surgical bed from January 1st, 2014 to December 31st, 2016. Statistical analyzes were performed with the SPSS 23.0 program. **Results:** Seventy patients who fulfilled the selection criteria were considered, of which 48.6% were HER 2 and 51.4% TN. After 36 months the local disease free survival (LDFS) was 85.7% vs. 100%in the teletherapy vs IORT arms and 92.9% vs 87.5% in HER2 and TN subgroups respectively; while the distant disease-free survival (DDFS) was 85.7 vs 100% in the teletherapy vs IORT arms and 96.4% vs 100%% in HER2 and TN respectively. **Conclusions:** Enhancing radiotherapy effect to the surgical bed with IORT using a 50 kV X-ray source during breast conserving surgery after neoadjuvant chemotherapy is at least not inferior to external radiotherapy. This approach offers benefit in local control, distance and overall survival in the scenario of enhancing doses to the surgical bed with IORT.

Session B – Oral presentations Dosimetry & Treatment Planning

Should in vivo dosimetry with GAFCHROMIC films during IORT for Accelerated Partial Breast Irradiation be performed for each treatment?

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Purpose: Comparison of the delivered dose to the prescribed IORT dose with in vivo dosimetry was performed. For intraoperative radiation therapy (IORT) using electrons in accelerated partial breast irradiation (APBI), this is especially relevant since a high dose is delivered in a single fraction. Moreover, there is no reliable image-based treatment planning system for IORT until now. **Materials and Methods:** For 39 elderly (60+) patients, diagnosed with breast cancer (tumour diameter < 3 cm) and treated with IORT in our institution, in vivo dosimetry was performed with GAFCHROMIC EBT3 films. APBI with a total dose of 23.3 Gy prescribed at 100% (21 Gy at 90%) was given during surgery according to the method described in the ELIOT study (1). All patients were irradiated with electron beams of 9 or 12 MeV generated with a dedicated IORT mobile accelerator (Mobetron 2000, INTRAOP, USA). A protection disk was used to shield the thoracic wall, the lung and the heart. During the dose measurements with GAFCHROMIC EBT3 films, the first and the second films were placed before and behind the protection disk, respectively (2). The calibration measurements were performed with the electron beams of the Mobetron 2000 in a water tank at the depth of dose maximum for each energy. Applicator output factors were determined relative to a 10-cm circular applicator, and the measurements were performed at dmax for each applicator and beam energy. According to the AAPM TG72 Report (3) recommendations, the applicator factors should be measured annually with a tolerance of 2-3%. **Results:** For the first 21 patients, the dose in breast tissue, measured with GAFCHROMIC films (mean value 23.89 Gy) was on average 2.4% (SD=2.6%, range -4.3% to 6.0%) higher than the prescribed dose of 23.33 Gy. After that applicator factors of the IORT accelerator were checked using an electron diode and a Roos ionization chamber. A small difference in comparison to those measured during the commissioning in 2016 was found, after which the applicator factors were altered adjusted accordingly. After this correction, the dose averaged over the following 18 patients (mean value 23.27 Gy) agreed within -0.3% (SD=1.9%, range -3.2% to 3.2%) with the prescribed dose. The mean dose measured behind the protection disk was within 0.46 Gy. **Conclusion:** Based on our results, we recommend to use GAFCHROMIC film dosimetry as a standard tool for patient quality assurance during breast cancer IORT and to check applicator output factors a few times per year for the mostly used applicator. In addition, in vivo GAFCHROMIC film dosimetry can monitor protection shield misalignment and display the isodose lines in front and behind the protection disk.

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Skin dose measurements in intraoperative breast treatments with radiochromic film. An update

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Objective: In intraoperatory breast cancer treatments the skin is the organ-at-risk. To measure skin dose, in 2016 we started to use Gafchromic ETB3 films to take advantage of their symmetrical construction and anti-newton ring coatings. As the films were in contact with the skin of the patients, they had to be sterilized. The aim of this study was twofold: First, to evaluate the effects of the sterilization process in the temporal stability of EBT3 films after the irradiation. Second, to measure the contribution to the skin dose of the tungsten drape placed over the patient to reduce scatter. **Material and Methods:** Four EBT3 radiochromic film sheets were used to evaluate the temporal stability. Two of the sheets were sterilized using plasma under 60º of temperature and a low pressure vacuum. The other two sheets weren't sterilized. Then, one of the sterilized pieces and one non-sterilized were placed in a patient and irradiated. The other two were kept as control. All of them were measured seven times over a period of one month in an Epson 10000 XL scanner, and then processed with Doselab. The influence of the tungsten drape in the skin dose was evaluated using an experimental setup that simulated clinical conditions. The INTRABEAM source was placed into a water phantom under which a 5 cm x 5 cm radiochromic film was placed and irradiated. The next step was to place the tungsten drape under the radiochromic sheet. Dose profiles measured from both sheets were compared to evaluate the differences between both setups. **Results:** Both irradiated sheets presented an increase in the absorbed dose with time that stabilized in about two weeks from the day of irradiation. The maximum differences were 26% in the case of the esterilized one and 23% in the case of the non-sterilized sheet. The non-irradiated non-sterilized sheet presented no changes with time, but the non-irradiated sterilized sheet developed as it was irradiated, stabilizing in the same time frame as the irradiated sheets. The maximum absorbed dose measured in this case was of 50 cGy. The mean differences between the dose profiles measured with the tungsten drape and without the drape was 8.3%, with a maximum difference of 10%. This increase in the absorbed dose can be attributed to the scattered radiation that is generated in the tungsten drape. **Conclusions:** The use of radiochromic film as a method to measure skin dose in intraoperatory breast cancer treatment is feasible and can easily be integrated in the surgical room procedure. However, the need for sterilization creates a complication in the preparation of the sheets. The 2 weeks period necessary for the films to fully develop and the small development of the sterilized sheets are a drawbacks that the users need to know. Finally, the tungsten drape should not be used, especially if the surgical room is big enough and/or structural shielding elements are present.

Real-time dosimetry for IORT procedures

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Objectives: Intraoperative Radiation Therapy (IORT) is a boosting technique where the tumor site is irradiated during surgery. IORT is demonstrated to be an effective boost strategy in breast cancer with excellent local control rates and low healthy tissue toxicity. It also improves the quality of life of the patient limiting the time spent for radiation treatments and the treatment costs. The main limitation of IORT lies in its uncertainties. A large source of uncertainty is the deposited dose, with possible consequences on the outcome of the treatment. In-vivo dosimetry offers the possibility to solve the issue in dose uncertainty by measuring the dose during or immediately after the treatment. Unfortunately, the currently used dosimeters are not designed for IORT, where aspects as minimal invasiveness, capacity to cope with large instantaneous dose rates and real-time capability are fundamental. We are testing a device based on optical fibers that will serve to monitor the amount of radiation dose deposited at given positions in the patient, in real-time. Optical fiber dosimetry is in general hampered by the so-called stem effect: when an optical fiber is exposed to radiation, a light

signal is produced along its length. This spurious signal overlaps with the signal generated in the sensitive part of the fiber (dosimetric sensor) and needs to be effectively suppressed, to obtain reliable dosimetric results. **Materials & Methods:** A rare-earth doped material was used to build a sensor on top of a PMMA optical fiber. The fiber has an external diameter of 1.3mm and the sensor has a length below 1mm. Preliminary clinical measurements were obtained in a water phantom, using a 6MeV Mobetron electrons accelerator, with a dose rate of 1000MU/min. The dose measuring device was optimized in a way that the stem signal originating from the fiber itself was below 2% of the dosimetric signal. **Results:** Our optical fiber based system, tested under clinical conditions, showed a satisfactory sensitivity, as well as a robust suppression of the stem effect. Our preliminary results show a good agreement with reference data in terms of relative depth dose profiles (PDD). Figure 1 shows the result of such a PDD measurement, performed on the Mobetron linear accelerator. **Conclusion:** Rare-earth based optical fiber dosimetry, thanks to their high light yield and favorable spectral properties, offer a true alternative to perform real-time optical fiber dosimetry, with effective suppression of the stem effect. These devices are characterized by minimal invasiveness, capability to work under high instantaneous dose rates and real-time performances. We are currently completing the development of a device that will allow real-time dose monitoring at multiple positions. We believe that our device will eventually increase the quality and safety of IORT treatments.

The photon contamination measurement from protective disks of electron beam intraoperative radiotherapy

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The aim of intraoperative radiotherapy is to deliver a high single fraction dose to a tumor bed during surgery. The use of electron beam in intraoperative radiotherapy is called intraoperative electron radiotherapy (IOERT) that is more common in cancer treatment due to its lower treatment time and the radiation safety of treatment in operating rooms. These mobile accelerators can safely work in almost any operating rooms with added little shielding or added no shielding. Concerning radiation protection of a patient organs at risk during IOERT, surgeon's use a specific radio protective disk under the normal tissue flap of a patient in order to protect the normal organs from the damage of radiation exposure especially in high energies of mobile linear accelerators. Due to the significant importance of radiation protection, the AAPM announced that in order to implement the IORT program in non-dedicated environment such as operating rooms, the radiation survey around the operating room (OR) and control area of IORT radiotherapy are mandatory to ensure that the maximum exposure limits are not exceeded from the safe maximum level. Although the photon scatter from the internal shielding plates with different material was measured, the photon contamination in control area of IOERT treatment with using the common radio protective disks are still unclear while the metal used in the disk composition increases the photon contamination and photon scatter during treatment. The aim of this study is to measure the photon scatter from PTFE-Stainless Steel and PMMA-Copper shielding plates during the IOERT treatment by practical dosimetry in 4 different energies of Liac (Info & tech, Roma, Italy, http://www.Sordina.com) portable device. Despite the fact that some research obtained the results on safety of IORT treatment in operating rooms, the data gathered in this study has shown that for safety of personnel using IOERT device, depending on the device workload, the portable shielding walls should be used during treatment procedure for safety of personnel.

Robust ^{192}Ir HDR IORT treatment planning and irradiation using the Freiburg flap

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Purpose: 192Ir IORT using the Freiburg flap is an alternative to kV-IORT and linac based IOERT. It is well suited to curved and deep seated anatomical regions such as the pelvis and skull. Robust and expeditious planning and irradiation minimizes sources of error and reduce operation duration. **Materials and Methods:** Our institute has a dedicated afterloader (microSelectron, Elekta AB Sweden) with a high activity (5-10Ci, 185-370GBq) 192Ir source located in a purpose built IORT operating theatre (OR), which also houses a Mobetron linac (IntraOp Sunnyvale CA) for IOERT. kV-IORT may be performed with the Intrabeam device (Carl Zeiss Meditec AG, Germany). Single leader catheters (Elekta AB 189.300) are employed with a radio-opaque button affixed to the distal end of the catheter. The Freiburg flap (Elekta AB 592.976) is cut to size in the OR, and may be sutured to the tumour bed. Radio-opaque buttons (Elekta AB 189.458) are placed at the proximal end of the catheter to affix the catheter relative to flap.Robust treatment planning is performed for rectangular (square) flaps using tabulated (homogeneous) dwell times, derived from extensive Oncentra Brachy (v4.3) calculations, [Ci.Gy-1] for 10mm source steps, prescribed at 10mm from the source axis (5mm in tissue). Calculated dwell times are entered manually into the TCS computer by an MPE. Consideration is given to the maximum (contact) dose at the surface of the silicon spheres, also tabulated for different flap sizes. Dwell times are verified by a radiation oncologist prior to treatment. A stainless steel measurement tool is employed to cut the catheters to the correct length and verify the length with the help of the internal kink protection. The latter provides a simple check to identify impassable channels. **Results:** Since 2013 we have performed 59 flap irradiations (119 IOERTs, 267 kV-IORTs): 50 flap irradiations (40 IOERTs, 267 kV-IORTs) since 2015. Treatment planning and irradiation is straight forward and insensitive to set-up errors, for example incorrect connection of afterloader channels. Moreover the planning and irradiation is expeditious which is advantageous in an OR with a heavy workload. However the dose distribution is inhomogeneous due to the limitations of the planning and the curvature of the flap in situ. The latter leads to under or overdosage at radii greater or less than the flap radius (perpendicular to the flap). **Conclusion:** We have described a robust technique for performing 192Ir IORT using the Freiburg flap. This technique has established itself as part of our clinical routine and found widespread acceptance with oncologists and surgical colleagues despite the relatively long irradiation times compared to IOERT. We are currently evaluating the possibility of individually optimizing treatment plans in the OR using Oncentra Brachy. This would enable more homogeneous dose distributions, irregular flap shapes and permit the definition of an integrated boost region.

Real-time dose computation algorithm for INTRABEAM

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Objective: The INTRABEAM (Carl Zeiss) system is a miniature accelerator for low energy X-rays Intra-Operative Radiation Therapy (XIORT), and it could benefit from a fast and accurate dose computation tool. With regards to accuracy, dose computed with Monte Carlo (MC) simulations are the gold standard, however they require a large computational effort and consequently they are not suitable for real-time dose planning. Accelerated codes such as DPM [1] aim to speed up this process, but they do not take advantage of modern and powerful GPUs. This work presents a GPU and/or multi-core implementation of a new dose calculation algorithm based in MC phase-space information to compute dose distributions for the INTRABEAM device within minutes, while fully considering the different structures of the patient and with the accuracy of realistic MC simulations. **Materials and Methods:** The GPU Hybrid Monte Carlo (GHMC) code is a GPU-based program that incorporates photoelectric, Compton and Rayleigh effects for the interaction of X-rays up to 1 MeV. Photon's attenuation coefficients are extracted from PENELOPE database [2], and Rayleigh and Compton scattering angles have been precomputed and stored for the different materials in a compact form. The code was parallelized to further increase the speed, and GPU encoded. Savings in computation

time are also possible by taking some variance reduction techniques to the extreme, such as the use of meta-histories, each one representing the fate of many particles, or dose normalization, which allows statistic noise-free dose distributions with a low number of initial meta-histories. Detailed MC simulations have been generated with penEasy [3] to validate our tool in homogeneous and heterogeneous conditions with the different INTRABEAM applicators. **Results:** Dose distributions computed by the GHMC are in good agreement with penEasy detailed simulations in homogeneous and heterogeneous media. The algorithm gives also good prediction of experimental dose distributions in water, and comparisons to measured data in heterogeneous phantoms are being carried out. Accurate dose distributions were obtained with the GHMC in minutes, compared to several days simulations with penEasy with a similar level of uncertainty. **Conclusion:** Implementing a dose computation code designed to take full advantage of modern GPUs makes it possible to obtain MC-grade accurate dose distributions within minutes. Its high speed allows a real-time dose calculation which includes the realistic effects of the beam in voxelized geometries of patients. It can be used as a dose planning tool in the operating room during a XIORT treatment with any INTRABEAM device.
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Total dose evaluation of a combined treatment of intraoperative and external radiotherapy.

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Purpose: To visualize the doses of intraoperative electron radiotherapy (IOERT) in an external radiotherapy treatment planning system (TPS) to take into account the previous irradiation in the future prescription of external radiotherapy and the limits to organs at risk, evaluating in a single computed tomography (CT) the contribution of both treatments. **Material and methods:** With Radiance TPS (GMV, Madrid, Spain), the doses of the IOERT treatments can be exported to patient's CT. With an external radiotherapy TPS, in our case RayStation version 6.1.1 (RaySearch Laboratories, Stockholm, Sweden), the CT and the treatment of IOERT are imported. Once in RayStation TPS, a rigid and a deformable registrations of the IOERT CT are performed with the new external radiotherapy CT. The dose of the IOERT treatment is then deformed to the new external radiotherapy CT. Afterwards we can observe the dose of IOERT in the external radiotherapy CT to be able to prescribe the new treatment of external radiotherapy, since the sum of doses of both treatments can be seen in the tumor volumes and in the organs at risk. The clinical case of a patient with combined treatment of IOERT and external radiotherapy in a locally advanced rectal cancer is presented in the images. **Results:** On the left side of the figure 1, it is shown the IOERT treatment in Radiance TPS in which a dose of 12.5 Gy was delivered to the presacral bed. The right side shows the external radiotherapy treatment with a dose prescription to the surgical bed and ganglion areas of 50.4 Gy with a first phase of 25 sessions at a dose per session of 1.80 Gy and a boost of 3 sessions of 1.80 Gy in the RayStation TPS. On the left side of the figure 2, it can be observed the deformable registration in RayStation TPS combining the IOERT CT with the external radiotherapy CT. On the right side, it is shown the deformed dose of the IOERT treatment on the external radiotherapy CT together with the subsequent treatment of external radiotherapy that was delivered. **Conclusion:** Radiance allows to export the IOERT treatment plan in order to evaluate the total contribution of the doses in the combined treatments of IOERT along with external radiotherapy.

Session C – practical medical aspects and research

Indications and clinical implications for the use of ^{192}Ir flap-IORT or IOERT

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Purpose: At our institution we perform 192Ir HDR (microSelectron, Elekta Ab Sweden)IORT using the Freiburg flap as well as IOERT (Mobetron, IntraOp, Sunnyvale,CA). In addition we perform kV-IORT (Intrabeam, Carl Zeiss Meditec AG)for partial breast irradiation. **Materials and Methods:** The indications for IORT are generally discussed in interdisciplinary tumour boards. The final decision for the use of IOERT or flap IORT is made by the radio-oncologist, respecting the anatomical site of the tumour bed , the need for radioprotection of structures in or near the tumour bed and taking into account the space for the electron tubus for instance in the bottom of the pelvis. **Results:** Since 2013 we have performed 59 flap IORTs (119 IOERTs, 267 kV-IORTs): Although flap IORTs generally require less time to set up in the operating theatre, and are more flexible for irradiating in deep seated highly curved anatomical regions, their irradiation times are longer than IOERTs. To date, we have observed no clinically relevant differences in the outcome , according to the technique. **Conclusions:** A clinical “decision-tree” for the use of IOERT or flap IORT will be discussed in the presentation. Both techniques have their advantages and disadvantages, but have established themselves in our institution.

Post Operative Complication After Lumpectomy with Intra Operative Radiation Therapy

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Background: Lumpectomy with intra operative radiation (IORT) is a relatively new treatment method for early breast cancer and by current guidelines is suitable for about 25% of newly diagnosed breast cancer patients. This method allows targeted radiation to the tumor bed, and obviates the need for external beam radiation (EBRT) in 85% of the cases. This treatment prevails in several medical centers in Israel and around the world, however, information regarding early and late post operative complications associated with the procedure is limited. **Aim:** To describe our experience with lumpectomy followed by IORT and compare complication rates and types of complications after the procedure with those seen after lumpectomy and EBRT. **Methods:** Clinical, demographic and histopathological data were collected from electronic medical records and a prospectively maintained database . Post operative complication were compared to those of women who had lumpectomy and EBRT during the same time period. **Results:** One hundred and three women who underwent IORT were included in the study. Average age was 67, and 10 patients had a prior lumpectomy with external beam radiation. Average follow up was 14 months. The most common complications were seroma (70 patients, of whom 14 underwent drainage), and erythema (33 cases, of which 23 were treated with antibiotics). In addition, 58 women suffered minor complications such as scar and breast deformity, edema, Mondor's syndrome and chronic pain. Only 15 women had no complications at all. Comparison to complication rates and types of complications after lumpectomy and EBRT will be presented. **Conclusions:** IORT is associated with a significant rate of postoperative complications, most of which are minor and transient.

Interim Update of the Targeted Intraoperative Radiotherapy United States (TARGIT-U.S.) Phase IV Registry Trial

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Background: Much of the evidence supporting targeted intraoperative radiotherapy (TARGIT) is derived from non-United States populations. Here we report the interim analysis of acute and chronic toxicity in a large cohort of U.S. women receiving TARGIT for early stage breast cancer. **Methods:** The TARGIT U.S. Registry trial is a pragmatic, prospective, non-randomized, multicenter registry trial. Women age 45 years and older with invasive ductal carcinoma were enrolled and received TARGIT at the time of breast conserving surgery. Whole breast external beam radiotherapy was also administered for women found to have unfavorable findings in their surgical pathology results, with TARGIT serving as the tumor bed boost. The primary objective of the study was to determine the rate of local recurrence. Secondary objectives included determination of treatment related acute and chronic toxicity and morbidity. Toxicity assessments were performed every six months after treatment for up to five years. **Results:** With median follow-up of 12.8 month (range 1 - 58), 657 patients were enrolled at 24 centers in the United States since May 29, 2012. 546 patients (83%) received TARGIT (20 Gy) at the time of breast conserving surgery. 111 patients (17%) received whole breast radiotherapy with TARGIT Boost due to unfavorable surgical pathology. Overall, 72.1% of patients identified as White, 5.7% as Asian, 10.5% as Black or African American, and 11.2% had unspecified race/ethnicity. Mean age was 66.4 years in the TARGIT group and 64.1 years in the TARGIT Boost group. More than 95% of patients were postmenopausal. Mean tumor size was 12.4 mm in the TARGIT group and 15.5 mm in the TARGIT Boost group. Negative margins were documented in 91% of patients in the TARGIT group and 69% of patients in the TARGIT Boost group. Patients in the TARGIT group were less likely to have high grade tumors (6.2% vs. 14.4%) or node-positive disease (8.1% vs. 36.9%). Seroma was the most commonly reported adverse event, but few seromas required radiologic or operative intervention (2.7% TARGIT vs 4.5% TARGIT Boost). Wound infection (3.2% vs. 4.5%) and hematoma (3.4% vs. 1.8%) were also infrequent in the TARGIT and TARGIT Boost groups, respectively. Delayed wound healing was reported in 1.3% of patients in the TARGIT group and 1.8% of patients in the TARGIT Boost group. Telangiectasias were not observed within the study. **Conclusion:** TARGIT is a safe method of delivering radiotherapy at the time of breast conserving surgery. Acute and chronic toxicity in this U.S.-based study is comparable to acute toxicity rates reported in the international TARGIT-A trial and other studies of partial breast radiation.

Feasibility of Intrabeam in Oncoplastic procedures in breast cancer surgery

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Objectives: Oncoplastic surgery: Unique approach focused on tumor resection and breast aesthetics to prevent deformities, minimize involved margins and reduce the potential local recurrence. An oncological disadvantage is when the surgical bed is closed and completely covered with glandular flaps. Then, it is often difficult to precisely locate the tumour when boost radiotherapy is needed. **Material and methods:** We will present three short videos of different oncoplastic techniques in breast cancer surgery: Grissotti Technique, Round Block lumpectomy and Oncological reduction pattern adding an intraoperative radiation with Intrabeam. **Results:** Intrabeam seams feasible in oncoplastic techniques in breast cancer surgery. It is necessary to apply intraoperative radiation treatment before to mobilize the flaps in the oncoplastic procedure. So, to irradiate the true tumor bed with Intrabeam in oncoplastic procedures is not only possible but more precise if it is done after surgery.**Conclusions:**
- Intraoperative radiotherapy with Intrabeam allows for precise localization of the tumour bed in

patients treated with an oncoplastic breast conservation procedure.
- The limiting factor is whether the Intrabeam applicator can be applied to the tumour bed while preserving a safe distance from the skin.
- A Phase II study has been designed to validate the feasibility of Intrabeam as a boost in oncoplastic procedures in patients whose RT treatment will be completed with hypofractionated whole breast RT.

Cosmetic results using oncoplastic surgical techniques to facilitate single dose electron based IORT.

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Purpose/ Objective: We report the post-treatment cosmesis of our single surgeon experience incorporating oncoplastic surgical techniques (OPS) to facilitate the delivery of electron beam intraoperative radiation (IORT). OPS avoids the poorly placed large incisions necessary to deliver the electron based IORT which may compromise long term cosmesis. **Materials and Methods:** Between April 2015 and August 2016, 31 patients with Stage 1 Luminal A breast cancer, bra size A to DD, underwent partial mastectomy using OPS to remove the tumor and deliver single fraction electron-based IORT to the tumor bed. All patients required placement of an 8 cm copper shield beneath the breast target tissue and a cylindrical delivery tube 5.5-6.5 cm over the target tissue, requiring large incisions to accommodate the devices. Fourteen patients underwent inverted T mammoplasty and 16 underwent modified Donut Mastopexy. One patient had an axillary approach. Donut mastopexy technique was used for patients with smaller and less ptotic breasts. Inverted T mammoplasty was employed with women who had larger and more ptotic breasts. Twenty-four of 31 patients had contralateral symmetrization at time of the index operation. Tumors were excised with negative margins. No patient had additional tissue excised for a breast reduction. All technical aspects of these cases including partial mastectomy, preparation of the field for IORT, breast reconstruction and contralateral symmetrization procedure were performed by a single breast surgeon. No patients withdrew from the study. **Results:** There were 3 complications, 1 patient required re-excision for a satellite DCIS lesion found on final path, 1 patient developed bilateral breast excoriations with delayed wound healing, 1 patient required surgical hematoma evacuation. Cosmesis was good to excellent in 29/31(93.5%) patients at 1 year determined by patients and 30/31 (96.8%) patients determined by MD evaluators. Average Cosmesis Score was pooled and analyzed using Mann-Whitney test, Kruskal-Wallis test, and Spearman correlation coefficients. There was no statistical correlation with any clinical characteristics nor surgical factors. There was no correlation of cosmesis score with addition of contralateral symmetrization procedure. Results were good to excellent regardless of patient characteristics or OPS technique used. The only statistically significant factor correlated with better cosmesis was time. Over the 1 year evaluated, both patient (p-value 0.039) and MD (p-value 0.0199) scores showed statistically significant improvement. **Conclusion:** Early results using OPS techniques to facilitate delivery of single dose electron based IORT appear promising in maintaining good to excellent cosmetic results. Cosmesis improved over time in a statistically significant manner. Further study is needed to determine if this trend in improved cosmesis will be maintained over time.

Use of electrons intraoperative radiotherapy in peripheral breast tumors through round block oncoplastic technique

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Mastology has gone through a great advances and changes in the management of breast cancer, from Halsted to the present, where the aim of the treatment for this pathology not only seeks to meet the oncological criteria of local control of the disease, but also to obtain better aesthetic results and contribute to optimize the life quality of patients, reducing the complications and side effects generated by the therapeutic alternatives. Oncoplasty represents a set of surgical techniques that are based on conservative management, decreasing the anatomical deformities of the breast, as well as immediate or delayed reconstruction. The round block technique consists of making a complete periareolar incision, de-epithelization of a peripheral circumference to the nipple areola complex; this allows a wide surgical field and an immediate reconstruction with excellent results. We propose the use of this technique for peripheral breast tumors, since it allows the placement of the different LIAC S® collimators for the application of the electrons intraoperative radiotherapy, allows to administer the complete or partial dose (boost) of radiation during the surgery, directly on the tumoral bed, the seat of 80% of the recurrences, diminishing the risk and the injurious effects on the skin. We'll describe the surgical technique that we use in our institution and make a review.

Oncoplastic surgery and intraoperative radiotherapy as a joint treatment in patients with breast cancer between the years 2014 - 2018 at the National Institute of Eoplastic Diseases - Peru

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INTRODUCTION: Intraoperative radiotherapy and oncoplastic surgery are two recent methods that have been gaining its space in the treatment of breast cancer, but both simultaneous procedures in order to obtain excellent aesthetic results in the treated patients are being applied recently generating some questions regarding feasibility, comfort and if the results obtained are similar or better than **conventional treatment. OBJECTIVES:** To evaluate the possibility of simultaneously applying intraoperative radiotherapy and oncoplastic surgery in patients with breast cancer. **MATERIAL AND METHODS:** we evaluated 32 patients with breast cancer diagnosis who had undergone conservation surgery (oncoplastic surgery + intraoperative radiotherapy) between April 2014 and January 2018. **RESULTS:** Of the 32 patients, 10 received IORT as a single treatment (Targit A) and 22 patients as Boost (Targit B). The average age was 61.1 years for patients classified as Targit A and 50.4 years for those of Targit B. All patients had infiltrating ductal carcinoma. Seven patients (31.8%) received neoadjuvant. During the surgical act, the time added to the surgery considered as the average irradiation time was 26.6 minutes [15-48]. The most commonly used spherical applicator was 3.5 cm in diameter (28%). The most frequent type of surgery was tumorectomy due to a non-visible incision 12 pacientes (38%), technical tumorectomy Round block 10 pacientes (31%), lateral pattern with replacement of nipple 4 pacientes (12.5%), vertical pattern 4 pacientes (12.5%), centralectomy 1paciente (3%), pattern grisotti 1paciente (3%). **CONCLUSIONS:** The IORT together with oncoplastic surgery is possible to perform in the treatment of breast cancer; we have noticed that the patterns of direct approach to the tumor are those that easily allow placing the applicator, allowing the procedure without major problem. It would be pending to evaluate if in the large oncoplastic resections where margins are bigger than 2 cm, the IORT plays a decisive role.

Session D – Oral presentations Physics & Biology

Influence of intra-operative radiotherapy (IORT) on tumor bed protein composition of exosome in breast cancer patients

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Background: Intra-operative radiotherapy (IORT) induces changes in tumor bed microenvironment specifically extracellular exosomes. Exosome-mediated macromolecules play important roles in modulation of radiotherapy. In this investigation used exosome protein profile detected by ITRAQ technique from the previous our study which demonstrated the effect of electron IORT technique (boost and radical doses) on tumor bed of patient with breast-conserving surgery before, immediately and 24h after IORT. **Methods:** Differentially expressed proteins (DEPs) were extracted from comparison between protein expressed in 24h after and before IORT. DEPs were analyzed by genetrail2 database to find cellular component category of gene ontology. Then selected extracellular exosome and analysis up and down-regulated proteins by constructing network and enriching biological process (BP) and KEGG pathways in string database, cytoscape software and enrichr database. **Result:** All exosome DEPs related boost treated group were 221 proteins in which 51 proteins were up-regulated. The most significant BPs activated was oxidation-reduction process and small molecule metabolism process. While inactivated process included neutrophil degranulation and important process associated with transcription, translation and repair. The KEGG pathways such as ribosome, metabolic pathway, proteasome, ECM-receptor interaction and biosynthesis of amino acids were inactivated or low moderated activity. In radical treated group detected 7 proteins of 289 DEPs up-regulated in exosome. The BP and KEGG pathways were same which inactivated in boost treated. **Conclusion:** Down-regulation of proteins in exosome derived from tumor bed tissue after IORT dysregulate the cellular process that influence cellular communication finally may eradicate remain tumor cells or metastatic cells.

The induction of radiation-induced subcutaneous fibrosis after intraoperative radiotherapy in breast cancer patients associates with epigenetic dysregulation

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Purpose/Objective: Late normal-tissue reactions limit the dose of radiotherapy (RT) given to cancer patients and affects their quality of life. Thus, the identification of patients with a predisposition for severe side effects before starting RT is a prerequisite for personalized treatment. For the treatment of breast cancer patients, RT-induced subcutaneous fibrosis is of high relevance, especially after intraoperative radiotherapy (IORT) given as an early boost before whole-breast RT (>30% fibrosis). Since the molecular mechanisms of fibrosis are not well understood, it was tested whether epigenetic regulation might explain inter-individual differences in fibrosis risk after IORT boost and if fibrogenic pathways could be modulated using drugs that modify epigenetic marks. **Materials and Methods:** Patients were treated with surgery and TARGIT IORT (20 Gy of 50 kV X-rays from Intrabeam) followed by external beam RT to the whole breast (46-50 Gy, 2 Gy fractions). Early-passage fibroblast cultures were established from skin biopsies taken from the upper arm before treatment. Fibroblasts from 45 patients without and 30 with fibrosis were included. Genome-wide DNA methylation profiling was performed using Illumina 450K arrays on 24 patient samples (12 with and 12 without fibrosis) and differentially methylated regions (DMRs) were validated by EpiTYPER MassARRAY. A variety of molecular and cell biological assays were performed to characterize a diacylglycerol kinase alpha (DGKA) DMR. Epigenetic modulation of this DMR was investigated using BET-bromodomain inhibitors

(JQ1, PFI-1). **Results:** An association with the fibrosis status was observed for 177 DMRs, 35 of which showed >10% methylation differences or ≥2 DMRs in one gene locus. Of these, the DGKA DMR was of special interest, as it was identified as an enhancer region. Reduced methylation of this DMR resulted in recruitment of the profibrotic transcription factor Early Growth Response 1 (EGR1) after radiation and promoted radiation-induced DGKA transcription in fibroblasts from patients who developed fibrosis after RT. Pharmacological inhibition or silencing of DGKA by siRNA resulted in a reduction of profibrotic cellular processes. The exposure of fibroblasts to BET-bromodomain inhibitors significantly reduced the bleomycin-induced increase in mRNA expression of DGKA down to baseline levels. Similar effects were observed for the fibrotic markers collagen I and α-smooth muscle actin.**Conclusion:** The present study shows that preexisting differences in the methylation status in the genome may affect the patient's susceptibility for developing fibrosis after RT. A number of DMRs were identified of which DGKA was functionally associated with profibrotic processes. In addition, a DGKA enhancer region could be modulated by epigenetic drug treatment. Interference with epigenetic patterns of fibrosis predisposition may provide novel preventive therapies that improve RT.

Investigation of cellular and molecular effects of intra operative X-Ray and Electron beam treated-wound fluid in Breast cancer patient

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Introduction: Post lumpectomy wound fluid, due to physiologic response to operation and also wound healing process; contains many growth of inflammatory factors. Tumor microenvironment play an important role in next cell fate decision, to select surviving and proliferation or death/senescence. **Purpose or Objective:** At this study we try to clarify cellular and molecular mechanism of growth arrest or cell death induced by IORT-treated WF and to compare effects of two type of IORT (electron vs photon based X-ray) on four type of breast cell lines. **Material and methods:** Drainage wf over the first 24 h after surgery were collected from each of 15 consecutive unselected breast cancer patient, each group is contained 3 patients, that undergo breast conserving surgery with or without IORT. According to our experiment we used both individual patient samples and pool of all fluids in every group. We used four type breast cell line, then we applied MTT assay for evaluation of proliferation, transwell assay for invasion, PI test for cell cycle, annexin v for apoptosis and ICC for MMP-9 and E-cadherin as tumorigenesis or tumor suppressor molecules. **Results:** our finding showed that proliferation process is not dependent to seroma concentration but over time different cells shows different proliferation response. Also MCF-7 cells had proliferant status particularly after 24L in all groups. In contrary SKBR-3 and MDA-MB-231 cells showed less proliferation response compared with MCF-7. So we can conclude that it is better to be evacuated post lumpectomy seroma in ER+/PR+ breast cancer patient, particularly 24h after operation. By receiving migrasion, invasion and colony assay, we can conclude that electron rays had better inhibitory effects on invasive cell lines, compared to X-Ray. In contrary, WF, wo-TORT attracted the cell to larger extent than the positive control. By reviewing apoptosis and senescence assays WF with and without IORT, has been better effects in inducing cell cycle arrest and death compared to control groups, but no significant difference between type of IORT and among with and wo-IORT group. **Conclusion:** Radiotherapy affects Breast tumor-bed tissue cell survival and also can modify TME by changing in cell phenotype, tissue molecular composition and cell-cell interactions. Radiotherapy not only have tumoricidal effect but also can alter TME; directly or Via produced and secreted molecules in tumor cavity, so could act as beneficial role in reducing local and distal recurrence rate.

Investigation of IORT-treated tumor bed modification in breast cancer via inducing biological pathways by new comprehensive approaches; Transcriptomic & Proteomic

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Introduction: The goal of radiation is to eradicate the remaining microscopic tumor cells. IORT can be applied to deliver irradiation to the cancer site, which delivers electron beams (IOERT) and low kv-x-ray. **Purpose or Objective:** In this study, for the first time and by our knowledge, we decided to investigate the biological effects of IORT in tumor bed of breast cancer in order to confirm the efficacy and beneficiency of IORT. We attempted to answer some clinical/biological questions: “Can IORT (12 and 21 GY) immediately modify tumor microenvironment phenotype by inducing challenges in different cell types with the notion of heterogeneity in tumor margin?” Dose timing can represent powerity of IORT in inducing above changes? Are these changes is related to the received two type of irradiation dose?” **Material and methods:** we used the newest comprehensive techniques in biology; RNA sequencing for transcriptomic study and quantification of proteins by iTRAQ for proteomics study. Six consecutive unselected breast cancer patient entered in our study. All patients were treated with IORT at the time of surgical resection with doses of 12 and 21 Gy and the samples categorized into three groups include: (1) MB; (2) MAi and (3) MA24h. A number of 18 RNA-Seq libraries were sequenced using Illumina HiSeq™ paired-end sequencing platform and 2X 150bp PE, ~20M Reads; ~6Gb Data for each samples were obtained from individual samples. **Results:** Local pathways such as apoptosis, cell death, DNA damage response, gene silencing, mesenchymal cell apoptosis, phagocytose, positive regulation of cell proliferation, migration, angiogenesis, neutrophil chemotaxis and epigenetics were enriched through IORT in parallel with systemic effects such as; cell metabolism, B-cell receptor signaling pathway and immune responses. All of these biological responses in tumor bed may be towards effectiveness of IORT. **Conclusion:** IORT after tumor excision have ability to use as safe and effective method in tumor margin control and about IOERT with two 12 and 21 Gy , have important local and systemic biological effects on disease control. Duo to IORT effectiveness it may be recommended as a standard method for breast cancer patients.

IORT dedicated linac radiation protection –new methods for an innovative approach

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Purpose: IORT dedicated Linacs operate inside not dedicated Operation Rooms. Even though there are currently more than 140 units installed worldwide, produced by different companies, there is currently no agreement on a standard approach dealing with how to define and measure their radiation protection features. A method based on NCRP Report No.151 and the Standard EN 60601-2-1 is proposed and applied to SIT latest model, LIAC HWL. **Material and Methods:** Stray radiation (SR) produced by IORT dedicated Linacs have been thoroughly analysed according to NCRP Report No.151 scheme. An innovative measurement method is proposed in order to define a standard and reproducible setup; such setup is intended to provide all the information needed for forecasting SR in any installation. Respect to the Operating Room where LIAC HWL is installed, SR has been measured in three different areas: patient or installation plane (90° respect e-beam direction), upstairs (180° respect e-beam direction), downstairs (0° respect e-beam direction). For each area the hot spot vs. the distance from the source is defined and measured; therefore the weekly workload calculation becomes a straightforward procedure. The patient has been simulated with a PMMA phantom 15 cm thick. The SR in patient plane (direction 90°) has been measured at 3 m from the target behind a drywall wall with variable thicknesses (1 to 7 cm); SR along direction 180° has been measured at a distance of 1 m from the radiant head according to the Fig.103 in EN 60601-2-1; SR downstairs has been measured along planes perpendicular to beam axis at two different distances 3 m and 2 m from the upper floor (standard concrete 30 cm). TVL along directions 0°, 90° and 180° have been

determined. Furthermore, a comparison between many survey meters has been performed in order to ascertain the most adequate ones: Inovision 451 B, Fluke 451P, Mirion DMC 3000, Canberra Babyline. **Results:** LIAC HWL behaves as a like point source in patient plane; this feature greatly simplifies RP calculus. At a distance of 3 m from the target, SR in patient plane results less than 0.2 uSv/Gy with 5 cm drywall wall; hotspot downstairs is less than 0,025 uSv/Gy at a distance of 3 m from upper floor (beam stopper diameter 70 cm, floor 30 cm thick); SR is less than 0,07 uSv/Gy at a distance of 1 m from the radiant head. **Conclusion:** Such procedure provides a reliable and effective tool for predicting SR in any installation; post installation surveys have proven the efficacy of such method. We hope the scientific community could study the subject and define new standards, so that users may benefit from specific, authoritative, and up to-date recommendations.

Clinical Implementation of pelvic intra-operative radiotherapy with flat applicators: dosimetric characterisation and clinical methodology

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Purpose: Very locally advanced rectal cancer remains a challenging clinical scenario. Positive resection margins lead to a very high risk of local recurrence, morbidity and reduced disease specific survival. In such cases chemoradiotherapy (CRT) is routinely given to reduce the size of the tumour and increase the probability of a clear resection margin. The treatment is given as fractionated external beam radiotherapy (EBRT), although data suggests that the dose required to sterilise a potentially positive resection margin exceeds 60Gy and higher than can be safely delivered with EBRT. Locally recurrent rectal cancer also represents a challenging clinical situation. Pelvic recurrence of rectal cancer gives rise to significant symptoms which greatly impact of quality of life. In each scenario IORT has been demonstrated to allow safe delivery of increased total biological equivalent dose relative to EBRT. **Material and Methods:** Two new flat applicators (3cm and 6cm diameter) were commissioned and dosimetrically characterised including depth dose measurements, uniformity and absolute dose verification. At the London Clinic hospital, a treatment protocol was developed to allow IORT doses up to 100 Gy BED for very locally advanced rectal cancer and a dose adapted approach for 80 Gy BED for locally recurrent cancer. This was used in conjunction with the Zeiss Intrabeam system and flat applicators. The work is expected to form the basis of a local registry study. **Results:** The first patient presented with resectable recurrent pelvic cancer was treated with IORT utilising the 6cm applicator. The IORT component was delivered during a total pelvic exenteration with extended lateral sidewall excision. A dose adapted prescription dose was devised according to the protocol to deliver a total dose of 100 Gy BED taking into account previous pelvic EBRT. Calibrated in-vivo dosimetry chips (OSLDs) were used to monitor dose to the sciatic nerve. **Conclusion:** Intra-operative radiotherapy for pelvic sites has been introduced at the London Clinic hospital. Two case studies are presented indicating successful delivery and patient outcome. The work is intended to form the basis of a future local registry study.

A new design for IORT filter to minimize backscatter and transmission dose in IORT

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Background: During IORT breast cancer treatment, in order to protect healthy tissues behind the tumour bed, radioprotection filters are currently used. The most widespread design of these discs entails a combination of two layers of different materials having relatively lower and higher atomic number (Z) in order to both stop the electrons after tumour bed and absorb the backscatter electrons and the bremsstrahlung x-rays. Such design has some limitations, as such disks cannot be used upside down and cannot always be sterilized in the sterilization machines. **Objective:** Our project aims

to demonstrate the functionality of an innovative radioprotection filter created from the combination of a biocompatible thermoplastic resin (TPR) and metallic shielding materials in an operational environment through the use of new materials and the 3D printing system to realise resistant, autoclavable, and symmetric radioprotection filters that are easy to use, in order to overtake the limits of the current filters. **Material and Method:** The new design has been assumed as a sandwich, with a high Z material placed between two layers of lower Z material and the whole disc is then covered by a biocompatible thermoplastic resin with the use of 3D printing technique. The characterization of the filter was made by Monte Carlo simulation technique with the use of MCNP code. Monte Carlo simulations were validated with the experimental percent depth dose (PDD) values. Simulations were made with two different beam energies (8 and 12 MeV). Different materials and their combinations were evaluated such as Aluminium (Al), copper (Cu), lead (Pb), Titanium (Ti) and steel. Al was used as lower Z material. For the purpose of comparison among different solutions and final evaluation of the disc, backscatter dose (%) and transmitted dose (%) compared to treatment dose values were selected as outcome. **Results:** In the study, over 10 different combinations of different metallic materials were tried in different geometric combinations, and three of them were selected as suitable. These combinations are TPR+Al+Ti+Al+TPR (T3), TPR+Al+Cu+Al+TPR (T5), TPR+Al+Steel+Al+TPR (T6). The results were compared with one of the most performant filters which are currently being used in the field (Al+Cu). For 8 MeV electron beam energy, the backscatter and transmitted radiation dose values are calculated in percent as respectively: 108%-0.4% for T3, 107%-0.3% for T5, 104%-0.3% for T6 and 108%-0.3% for the filter consisting of 6mm Al+ 3mmCu. From the results it can be seen that T6 combination displays better radioprotection characteristics than the Al+Cu filters. **Conclusions:** The new design proposed reduces the backscatter and the transmitted dose and cancels the possibility of misplacement (i.e. upside-down positioning) of the filter during IORT application. Furthermore, it will be easier to sterilize without the need for a sterile sheath.

Session E – Oral presentations various tumor sites

Combination of perioperative chemotherapy and intraoperative radiotherapy for the treatment of resectable intrahepatic cholangiocarcinoma

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Introduction: A new treatment method involving neoadjuvant hepatic chemoembolization 5 days prior to surgery combined with intraoperative radiotherapy (IORT) followed by adjuvant chemotherapy was established for patients with resectable intrahepatic cholangiocarcinoma (ICC). The aim of the present study was to assess the safety and efficacy of this treatment scheme. **Method:** Records of 24 patients with resectable ICC treated in Botkin Hospital between 2015-2017 were reviewed. In all cases was used perioperative chemoradiotherapy (PeriCRT). IORT was performed using Carl Zeiss Intrabeam PRS 500 system. After chemoembolization, resection stage, a single dose of 20 Gy IORT was delivered using 50-kV x-rays to a depth of 1 mm from the applicator surface. Afterward a histological examination and electron microscopy of irradiated resection margin were performed. **Results:** All 24 patients with ICC underwent gross total resection (R0) with lymphadenectomy. The estimated median survival was 20 month. Long-term survival was 80,1% (PeriCRT) for 3-year survival, respectively ($p< 0,05$, 95% CI). All treatment methods were well tolerated by all patients, with few adverse effects and no serious complications. There was no association between outcomes, variations in tumor characteristics, marker concentrations and therapeutic response.**Conclusions**: Good 3-year OS for resected ICC was achieved by using novel PeriCRT treatment method.

Intraoperative high-dose-rate brachytherapy using the Freiburg flap

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Between March 2016 and March 2017, thertyfive patients received IOHDR brachytherapy using the Freiburg flap at the time of surgical resection. Of these patients 33 had sarcomas, 1 had Merkel cell carcinoma and 1 had melanoma. The mean age was 63.4 years (range 33-93). Negative margin (R0) was obtained in 14 patients and microscopically positive margins (R1) in 1 patient. Twelve patients received postoperative external beam radiation therapy (EBRT). The IOHDR dose was 15 Gy in 23 patients and 12 Gy in 12 patients and the mean EBRT dose was 46.7 Gy (range 44-54 Gy). **Results:** With a mean follow up of 13.51 months (range 3.83-18.93) the local control was 100%. There were no G3-4 intraoperative o postoperative complications. Acute toxicities were wound infection in 3 patients and poor healing with wound dehiscence in 5 patients. No late toxicities were seen. **Conclusion:** IOHDR brachytherapy using the Freiburg flap is a feasible, save and well-tolerated component of multimodally therapy for different types of tumours. Allows dose escalation in a well-defined intraoperative surgical bed, separating or protecting the organs at risk, reducing EBRT dose and the side effects. Although the results are encouraging we need further follow up.

Local tumor control and long-term overall survival in 47 patients with anterior skull base tumors treated with intraoperative radiotherapy

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Purpose/Objective(s): In this retrospective analysis we provide long-term follow-up data on 47 patients with anterior skull base tumors treated with electron-based intraoperative radiotherapy (IOERT) over a 17-year period. We evaluated whether IOERT is a viable treatment option in this sensitive anatomical area and if local control and survival could be improved with this treatment modality compared to historical controls. **Materials/Methods:** 36 male and 11 female patients between 35 and 73 years of age were treated. The histology consisted of squamous cell carcinoma (30 pts.), adenocarcinoma (11), undifferentiated (4), adenoid cystic carcinoma (3), olfactorius neuroblastoma (3), neuroendocrine and mucoepidermoid carcinoma (2 each), and nasopharyngeal carcinoma Schmincke, leiomyosarcoma, basalioma, melanoma, transitional cell carcinoma and sebaceous gland carcinoma (one each). After local tumor excision with different open surgical procedures, IOERT was given in 47 patients: 29 treatments for primary cancer and 18 for recurrent tumors. A maximum dose of 10 Gy was applied with perplex tubes (diameters 4 - 5 cm) and electron energies between 4 and 6 MeV. 33 Patients also received adjuvant external beam radiotherapy (EBRT) with a mean dose of 56.4 Gy (SD 8.83, range 30-71.2 Gy) The anatomical areas most often involved were the paranasal sinuses (26 primaries, 5 recurrent tumors) followed by nasal cavity (6), nasopharynx (2), buccal mucosa (2),oropharynx (2),orbita (2), parotid gland (1) and recurrence of unknown H&N CUP. **Results:** With a median follow-up of 5.7 years (0.1-17 years), 12 of 29 patients with advanced primary tumors and 6 of 18 patients with recurrent tumors are alive. Of these, 14 patients have a survival of at least 100 months with local and distant control. Two further patients are controlled locally without distant disease at 77 and 54 months, two patients are locally controlled at 59 and 30 months, but show distant metastases. Out of 18 patients with locally controlled tumors, 15 had also received adjuvant EBRT. 29 patients have died after a mean survival time of 30.2 mths. (1-97) for the following reasons: 9 from local progression, 10 from metastases, 5 patients from secondary malignancies and 5 from intercurrent diseases. Four out of 9 local recurrences developed within the IOERT field, the remaining 5 were noted as marginal/outside. In total, 20 patients at the time of death remained free of local tumor. **Conclusion:** To date, this cohort of 47 patients treated with IOERT +/- EBRT at the anterior skull base represents the largest group of patients treated with these treatment modalities. Inclusion of intraoperative radiotherapy in the interdisciplinary treatment of these patients with advanced primaries and recurrent tumors led to long-term local tumor control in 80% of patients

and thus to long-term survival in one third of patients, both results comparing favorably to historical reports.

Feasibility of Dose Escalation Using Intraoperative Radiotherapy Following Resection of Large Brain Metastases Compared to Post-operative SRS

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Background/Purpose: Dose reduction is used for increasing tumor volumes in stereotactic radiosurgery (SRS) due to risks of radiation injury reaction with increasing tumor diameter. This concept runs contrary to the general principles of oncology, where more tumor should not require less dose, and this may contribute to increases in local failure which approaches 40% in prospective studies for surgery followed by SRS. Thus alternative strategies are warranted. We hypothesize that the steep conformal fall off inherent to intra-operative radiotherapy (IORT) will afford dose escalation over SRS without increasing dose to critical structures. **Methods/Materials:** Five consecutive patients treated with surgical resection followed by IORT using Zeiss INTRABEAM spherical applicator system to deliver 30Gy to applicator surface for large brain metastases from 10/2017 to 11/2017 were retrospectively reviewed. Using the post-operative MRI, single fraction SRS plans were created for the Perfexion™ Gamma Knife system using GammaPlan® v10.1. SRS plans were generated both for marginal doses of 15-18Gy in 1 fraction as dictated by the resection cavity volume per NCCTG N107C dose guidelines as well for 30Gy marginal dose as used for IORT. Critical organ dosimetry and the total volume of brain receiving 12Gy were calculated for IORT and SRS. Critical organ dosimetry was compared using paired t test. A $p < 0.05$ was considered significant for all comparisons. **Results:** Median patient age was 67 (IQR:65-75), median RPA class was 2 (2-2), and median SRS gross tumor volume was 15.6cc (IQR: 7.6-18.5). The most common primary histology was non-small cell lung cancer in 60%. Applicator size ranged from 1.5-3.0cm. The mean V12Gy volume for IORT was 21.32cc +/-0.58 versus 26.89cc +/-10.06 for SRS marginal doses of 15-18Gy, p=0.31, and 68.65cc +/-30.56 for SRS doses of 30Gy, p=0.02. The mean maximal dose for the brainstem for IORT was 0.45Gy +/-0.52 versus 1.10 +/-0.85 for SRS marginal doses of 15-18Gy, p=0.03, and 2.02Gy +/-1.71 for SRS doses of 30Gy, p=0.04. The mean maximal dose for the optic apparatus for IORT was 0.38Gy +/-0.21 versus 0.54 +/-0.21 for SRS marginal doses of 15-18Gy, p=0.27, and 0.98Gy +/-0.43 for SRS doses of 30Gy, p=0.03. **Conclusions:** IORT allows for dose escalation up to 30Gy to applicator surface with comparable or lower doses than that clinically achieved with dose ranges of 15-18Gy commonly used with post-operative SRS and significantly lower than that delivered with SRS to achieve marginal doses of 30Gy. Continued follow-up is warranted to assess toxicity and tumor control.

IOERT in locally recurrent high grade RPS: a retrospective single center analysis of 83 cases

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Background and Purpose: To report our experience with surgery and intraoperative electron radiation therapy (IOERT) with or without external beam radiation therapy (EBRT) in patients with locally recurrent high-grade retroperitoneal soft-tissue sarcoma (RPS). **Patients and Methods:** We conducted a retrospective evaluation of patients with RPS who have been treated with IOERT at our institution since 1991. Patients treated for primary disease, suffering from low grade tumors or with distant metastases were excluded, leaving 83 patients for the final analysis. Median tumor size was 9 cm with undifferentiated liposarcoma being the dominating histology (61%). Lesions were grade 2 in 34% and grade 3 in 66%. Surgery resulted in gross complete resection in 94%, but only 19% had microscopic negative margins despite multivisceral resections in 58%. All patients had IOERT with a median dose of 15 Gy, 53 patients (64%) received additional perioperative EBRT (23% preop., 77%

postop.) with a median dose of 45 Gy. **Results:** Median follow-up for the entire cohort was 35 months and 43 months in surviving patients. Estimated 5-year-LC was only 35%. In univariate analysis, LC was significantly associated with UICC stage while only trends were present for grading, T stage and addition of EBRT. In multivariate analysis, only grading (5yr-LC G2 59% vs G3 22%) was found to be a significant factor regarding LC. Estimated 5-year OS was 48%. In univariate analysis, OS was significantly associated with grading and resection margin. Interestingly, only the achievement of gross total resection (GTR) was beneficial (5yr-OS GTR 55% vs no GTR 0%), while microscopic margin status (R0 vs R1) did not influence OS significantly. In multivariate analysis, GTR remained the only significant factor for OS. **Conclusions:** Outcome of recurrent high grade RPS was clearly worse compared to primary cases even after combination of surgery, IORT and EBRT. Reasonable efforts should be made already during primary treatment to prevent the onset of local recurrences. Prognostic factors may differ from primary cases and should be transferred with caution. GTR remained the only factor with significant impact on OS in multivariate analysis.

IOERT in primary retroperitoneal sarcoma: a retrospective single center analysis of 69 cases

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Purpose: To report our experience with surgery and intraoperative radiation therapy (IOERT) with or without external beam radiation therapy (EBRT) in patients with primary retroperitoneal soft-tissue sarcoma (RPS). **Materials and Methods:** We conducted a retrospective evaluation of patients with RPS who have been treated with IOERT at our institution since 1991. Patients treated for recurrent disease were excluded, leaving 69 patients for the final analysis. Median tumor size was 12.5 cm, most lesions were high grade (79%). Main histologies were as follows: well-differentiated liposarcoma 15%, leiomyosarcoma 26%, dedifferentiated liposarcoma 38% and others 22%. Surgery resulted in gross complete resection in 90%, but only 36% had microscopic negative margins despite multivisceral resections in 64%. All patients had IORT with a median dose of 12 Gy, 58 patients (84%) received additional perioperative EBRT (45% preop., 55% postop.) with a median dose of 45 Gy. **Results:** Median follow-up for the entire cohort was 39 months and 54 months in surviving patients. Estimated 5-year-LC was 71%. In univariate analysis, LC was significantly associated with resection margin (5-year LC R0: 94%, R1: 52%, R2: 31%). Trends were present for gender, grading, and UICC stage. In multivariate analysis, only resection margin remained significant. Estimated 5-year OS was 63%. In univariate analysis, OS was significantly associated with grading, UICC stage, resection margin and timing of EBRT (5-year OS preop. 91% vs postop. 47% vs none 63%). In multivariate analysis, only timing of EBRT remained significant. Interestingly, neoadjuvant EBRT seemed superior while postoperative EBRT did result in even worse survival than no EBRT. C**onclusions:** Combination of surgery, IORT and EBRT resulted in very promising local control and survival. Complete resection remains the cornerstone of treatment as margin status was associated with local control and survival. EBRT should be preferably applied preoperatively.

Intraoperative radioterapy (IORT) in the multimodality treatment of locally advanced prostate cancer

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PURPOSE: The treatment for locally advanced prostate cancer is a controversial issue and multimodality treatment can lead to treatment optimization. The aim of this study is to describe technical and clinical aspects of intra-operative radiotherapy (IORT) in patients with high risk prostate cancer. **MATERIAL/METHODS:** A total of 136 patients were enrolled. The statistical analysis was performed in 112 patients with follow up > 12 months. Inclusion criteria were patients age < 76 years, KPS > 90 and at least 2 of the following preoperative risk factor: initial PSA (iPSA) > 10 ng/ml, Gleason Score ≥ 7, clinical staging > cT2c according with TNM, probability of organ-confined disease < 25%. Median age was 66.9 years (range 51-83), median iPSA was 14.8 ng/ml (range 2.0-154) and median Gleason Score (GS) was 8 (range 4-10). After surgical exposure of the prostate, IORT was delivered by a dedicated linear accelerator (Mobetron, Intraop, Sunnyvale, CA) with 30° beveled collimator, using an electron beam of 9-12 MeV to a total dose of 12 Gy. IORT was followed by radical prostatectomy and regional lymph node dissection. Rectal dose was measured “in vivo” by radio-chromic films placed on a rectal probe. All cases with pathological staging≥ pT3a, positive margins (R1) or metastatic lymph nodes (N1) received postoperative external beam radiotherapy (EBRT), delivered to surgical bed with 3D conformal technique or intensity modulated radiation therapy to a total dose of 46-50 Gy (2Gy/fraction). Patients with pT3 or pT4 disease and/or N1 received adjuvant hormonal therapy. **RESULTS:** IORT procedure lasted in average 30 minutes (range 15-50). No major intra- or post-operative complication occurred. Median dose to the anterior rectal wall was 4.32 Gy (range 0.06-11.3). Pathological stage was: 32 pT2, 97 pT3, 7 pT4. 83/136 (61,0%) patients were R1 and 45/136 (33,1%) patients were N1. Median post-operative PSA was 0.09 ng/ml (range 0-5.05). Post-operative radiotherapy was delivered to 106/136 patients (77.9%) with pathological staging ≥ pT3a or R1. Hormone therapy was prescribed to 88/136 patients (64.7%). Acute toxicity was: 22 G2 (12 GU; 10 GI), 3 G3 (2 GU; 1 GI). Late toxicity was: 11 G2 (5 GU, 6 GI), 4 G3 (2 GU; 2 GI). No G4 acute or late toxicity was observed. Twelve patients died of prostate cancer. With a median follow-up of 81 months (range 12-132), 34/112 patients experienced biochemical failure. Overall biochemical free survival (BFS) was 60% at 5 years. 5 years BFS was 81% and 55 % in high and very high risk classes according to NCCN classification. No macroscopic failure in the prostate surgical bed was observed. **CONCLUSIONS**: IORT during radical prostatectomy is a feasible procedure and allows to deliver safely post-operative EBRT to surgical bed without a significant increase of toxicity. With a median follow-up of 81 months, biochemical control seems to be optimal in particular for high risk patients.

Phase I/II trial of surface kilovoltage bra chytherapy in ocular conjuntival carcinoma: Preliminary results

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Purpose: To determine the safety dose and toxicity profile of adjuvant kilovoltage brachytherapy in post resected ocular conjunctival carcinoma. **Materials and methods:** Between October 2014 and June 2017, at the National Institute of Neoplastic Diseases from Peru, 39 patients with squamous cell carcinoma of ocular conjunctiva, T1 - T3, resected, were selected to adjuvant treatment. The portable accelerator of 50 kV INTRABEAM® (Carl Zeiss Meditec) was used, previous local anesthesia and blocking of ocular muscles movement. The doses used were 18 Gy for patients with free margins and 22 Gy for positive edges, according to calculation of equivalent dose of 2Gy per fraction of 46 and 66 Gy respectively, assuming a tumoral α/β ratio of 8 Gy. The prescription was done to 2 mm depth.

Results: The median age was 69 years, distributed evenly between both genders, with a median follow-up of 12 months. The surgical margins were 59% free and 41% committed, with no difference between the institutions where the surgery was performed (p = 0.069). The median of tumor size was 7 mm with 2 mm of invasion, 61.5% was T2 and 35.9% T1. The mean time between surgery and irradiation was 1.5 months, 23.1% of patients developed grade I toxicity of spontaneous resolution, without evidence of greater degree in any case. The dose had no statistical relationship with toxicity (p = 0.533). One-year disease-free survival was 96.7%. **Conclusions:** Kilovoltage surface brachytherapy is an applicable and reproducible tool in the treatment of squamous cell carcinoma of ocular conjunctiva. The administered doses are safe and well tolerated by patients with low levels of acute toxicity. Longer follow-up is needed to establish disease control rates and late toxicities.

IORT in Recurrent Salivary and Cervical Cancers

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Purpose or Objective: The purpose of the present study was to review experience with the use of IORT for primary or recurrent malignancies of the parotid gland and the neck. **Material and Methods:** We retrospectively reviewed 327 patients treated with IORT. 231 had recurrent cervical cancer and 96 were treated for primary or recurrent cancer of the parotid gland. The median age was 62.9 years (range, 14.3-88.1). IORT was administered as a single fraction to a dose of 15 Gy or 20 Gy in most pts. The majority was treated with 5 MeV electrons.The median follow-up period was 5.6 years. **Results:** The recurrence-free survival rate at 5 years for neck and parotid gland patients were 65.2% and 49% respectively. The 5-year overall survival rate after surgery and IORT were 56.2% and 26% respectively. No perioperative fatalities occurred. Common complications were vascular complications, fistulas, radiation osteonecrosis, flap necrosis, wound dehiscence, and neuropathy . The majority of recurrences were regional. **Conclusion:** IORT results in effective local control at acceptable levels of toxicity in patients with recurrent cervical and salivary gland malignancies.

Session F – Clinical Trials

Intraoperative Electron Beam Radiotherapy (IOERT) for Locoregional Peristent or recurrent head & neck carcinomas

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Purpose: To report our institutional experience with Intraoperative Electron Beam Radiotherapy (IOERT) for persistent or recurrent head and neck cancer. **Methods and Materials:** 61 patients were treated with salvage surgery and IEORT. 58 patients (95%) had previously received external beam radiotherapy (EBRT) as a component of their definitive therapy. 44 patients (72%) had squamous cell histology (SCC). Surgical margins were positive in 28 patients (46%). IEORT was prescribed to a median dose of 12.5 Gy (range, 10 - 17.5). 23 patients (38%) received a course of post-operative EBRT (median 45 Gy). Clinical outcomes were retrospectively reviewed and univariate analysis was performed using log-rank tests to correlate clinical outcomes with histology, surgical margin, and adjuvant therapy. **Results:** Median follow-up among surviving patients was 15.9 months. Median progression free survival (PFS) and overall survival (OS) were 9.8 and 19.1 months, respectively. 1 and 2-year rates of locoregional control (LRC) were 59% and 35%, respectively. 1 and 2-year rates of PFS are 39% and 19%, respectively. 1 and 2-year rates of OS were 62% and 42%, respectively. Overall survival was better for non-SCC histology (p = 0.03). For SCC patients, negative surgical margin showed a trend toward improved PFS (p = 0.09) and OS (p = 0.06). There was one grade 5 toxicity due to carotid rupture. **Conclusions:** IOERT has shown effective LRC and OS with an acceptably low rate of severe toxicity at our institution. OS was significantly better for non-SCC

histology. For SCC patients, there is a trend toward improved PFS and OS associated with negative surgical margins.

ISIORT pooled analysis 2018: characteristics of intraoperative radiotherapy in 12,678 patients

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Purpose: Data from centres active in intraoperative radiotherapy (IORT) were collected within the International Society of Intraoperative Radiotherapy (ISIORT) program. The purpose of the present analysis was to analyse and report the main clinical and technical variables of IORT performed by the participating centres. **Materials and Methods:** In 2007, the ISIORT-Europe centres were invited to record demographic, clinical and technical data relating to their IORT procedures in a joint online database. **Results:** 12,678 IORT procedures from 45 centres have been recorded from 2007 to 2018. 96% of treatment was performed with electrons, while 496 treatments were performed with x-rays. Median age of patients was 68 years (range: 5 months – 89 years). Gender was female in 81.2% of cases and male in 18.8%. Treatments were curative in 12,167 cases (94.1%) and 3,077 (23.8%) cases were included in study protocols. The most frequent tumour was breast cancer with 9,879 cases (76.4%) followed by rectal cancer with 1,073 cases (8.3%), soft tissue and bone sarcomas with 414 cases (3.2%), prostate cancer with 194 cases (1.5%), gastric cancer with 142 cases (1.1%) and pancreatic cancer with 141 cases (1.1%). **Conclusion:** Treatment chronology shows how IORT number of recorded cases increased according with the interest in this ISIORT project. This survey gives an overview of worldwide use of IORT including patient selection criteria and treatment modalities and could represent a basis to design future clinical trials.

Poster

Intra-operative radiotherapy (IORT) for treatment of locally advanced esophageal cancer: preliminary results in a series of 17 patients.

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Purpose: to describe our experience with intraoperative radiotherapy (IORT) as a boost after preoperative chemo-radiotherapy (RT) in patients with locally advanced esophageal cancer. **Materials and Methods:** Seventeen patients (pts), median age 61 years, with locally advanced esophageal cancer were enrolled in our institutional protocol and underwent pre-operative chemo-radiation therapy followed by surgery with IORT boost. Tumor locations were: 2 in upper, 11 in middle and 4 in lower esophageal third. Pathology was squamous cell carcinoma in 15 cases and adenocarcinoma in 2 cases. Clinical stages were: 2 pts stage II, 13 pts stage III and 2 pts stage IV. Pre-operative radiotherapy was prescribed with conformal technique by using 6-15 MeV X-rays to a total dose of 44 Gy in 22 fractions (2 Gy/fr) and one patient to total dose of 41,4 Gy in 23 fractions (1,8 Gy/ fr). Chemotherapy was given concomitantly to radiotherapy with cisplatin and 5-FU and in one case with carboplatin and taxol. IORT was performed after surgical resection to the tumor bed and/or regional lymph nodal areas by a dedicated linear accelerator (Mobetron, Intraop, Sunnyvale, CA). A single dose of high-energy electrons (6, 9 or 12 MeV) of 10-15 Gy was delivered by collimator (3-5,5 cm) with bevel 0°-30°. Procedure timing was 20-25 minutes.**Results:** one of 17 pts received only preoperative RT for severe renal failure and one patient required in urgency surgery for mediastinitis. Four pts developed chemo-related toxicity. Surgery consisted of total or sub-total esophagectomy with lymphadenectomy. One patient died during surgery for massive bleeding; two pts died just after the surgery for pulmonary embolism and gastric necrosis. Postoperative complications occurred in 7/14 cases and consisted of pulmonary embolism, gastro-tracheal fistula, mediastinitis, respiratory distress. Median follow up was 24 months (range 1-92). Survival rate at 1, 2, 4 years was 71%, 50% and 40%, respectively. Causes of death were: 1 pulmonary embolism, 1 pulmonary distress,1 cardiac failure and 10 progression disease with distant relapse, only 2 cases of these (20%) showed regional recurrences after 11 and 21 months from surgery. **Conclusion:** IORT during surgery for esophageal carcinoma seems to be a feasible procedure combined with preoperative chemo-radiotherapy, although toxicity is not negligible. Larger number of patient and longer follow-up are needed to assess long-term outcome.

Intraoperative radiotherapy optimizes conservative treatment of breast cancer with advantages in quality of life and work resumption

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Objective: Intraoperative radiotherapy (IORT) could be not-inferior to external beam radiotherapy (EBRT) in accurately selected patients. Other important outcomes such as toxicities, self-perception of body image, quality of life, and resumption of work or daily activities were poorly explored. The aim of the present study was to compare these outcomes between EBRT, IORT full-dose (IORT-f) and IORT boost (IORT-b). **Material and Methods:** A total of 443 consecutive patients, candidates for breast-conserving surgery, were included: EBRT was performed in 220 patients (49.7%), IORT-f in 140 patients (31.6%), and IORT-b in 83 patients (18.7%). Data on treatment-related toxicities were collected. Patients were evaluated at 6 months to assess possible changes in self-perception of body image and limitations with the Breast Cancer Questionnaire (BIBCQ). A second questionnaire

explored the impact of EBRT, IORT-f and IORT-b on resumption of work and normal daily activities. **Results:** EBRT carried a higher risk of breast fibrosis and retraction (OR 3.58, 95% CI 1.024-12.526, p = 0.046) and breast edema (OR 6, 95% CI 2.077-17.335, p=0.001) compared to IORT-f, but a lower risk of seroma compared to IORT-b (OR 0.36, 95% CI 0.166-0.785, p = 0.01). The BIBCQ scores showed a better outcome in arm concerns with IORT-f (-3.3, p = 0.006) and IORT-b (-1.3, p = 0.002) vs. EBRT (-1.7), although the higher rate in axillary dissections in the latter could be a bias. Median time to return to daily activities was 70.6 days with EBRT vs. 41 days with IORT-f (p < 0.0001) and 53.3 days with IORT-b (p = 0.07), without any effect of age or axillary dissection. **Conclusions:** IORT could be an advantageous radiotherapy approach for carefully selected patients, reducing post-treatment sequelae related to whole-breast irradiation. Our findings suggest that IORT allows a faster resumption of work and daily activities, especially in workers that could represent the majority of breast cancer patients in a near future.

Our intraoperative radiotherapy experience

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Purpose: To present our 5'year experience and case selection criteria for intraoperative electron radiotherapy (IOERT) as Boost, that significantly reduces the local recurrence rate after breast conserving surgery in patients with breast cancer. **Material and Methods:** Early stage breast cancer patients (n:103), who were suitable for IOERT were identified within the group of patients who were selected for breast conserving surgery at our breast council. The MOBETRON ((IntraOp Medical,USA):mobile linear accelerator for IOERT) was used during surgery. **Results:** Patients (n:103) with early stage breast cancer in one focus (or two foci within 2 cm), with a histologic grade of 2–3, and a high possibility of local recurrence were admitted for IOERT application. Informed consent was obtained from all participants. Lumpectomy and sentinel lymph node biopsy was performed, and advancement flaps were prepared according to the size and inclination of the conus following evaluation of tumor size and surgical margins by pathology. Distance to the thoracic wall was measured, and a radiation oncologist and radiation physicist calculated the required dose. Anesthesia was regulated with slower ventilation frequency, without causing hypoxia. The skin and incision edges were protected, the field was radiated. Once focusing was complete, an electron equivalent to 10 Gy was applied via MOBETRON using a conus of an average diameter of 5.4 cm (range, 4–7 cm), with an average 865 (773–954) monitor unit (MU) and 90% reference isodose with 6 MeV energy, which was selected based on the status of the patient. Mean age of patients was 53 (37-68) years; mean follow-up was 35 months (2-58); tumor diameter was 18 (4–30) mm; and lymph node involvement was observed in 11 patients. Histological analysis revealed 90 invasive ductal carcinomas, 8 invasive lobular tumors and 5 mixed structure. The Boost area was planned, so as to cover 15–20 mm of the surrounding tumor bed area. In the postoperative period, 46 patients received chemotherapy first, followed by WBRT, and 57 patients only WBRT.87 Cases. A total of 87 cases received hormonotherapy. Local recurrence was not detected and there were no major postoperative surgical or early radiotherapy related complications. **Conclusion:** The completion of one stage of local therapy with IOERT during surgery positively effects sequencing of other treatments like chemotherapy, hormonotherapy and radiotherapy, It can also increase the quality of service provided to the patient (and other patients) by partially reducing the workload.

Quality assurance and organ at risk dosimetry during low energy x-ray in IORT treated breast cancer

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Purpose: At this study we try to evaluate the absorbed radiation dose at organ at risk, during IORT in breast cancer by using EBT3 radiochromic film. **Material and methods:** Nowadays, IORT technique is used for tumor bed irradiation after BCS. Low x-ray IORT is used in intrabeam system. In this technique, tumor bed irradiation via spherical appapplicatn with 20 Gy irradiation dose. Because of no suitable treatment planning system, evaluation of safely of treatment and also received dose at organ at risk is very important. EBT3 radio chromic film is used for invivo dosimetry. At first, by using ion chamber and water phantoms, we calculated calibration curve of this film in two red and green channel and in two periods (zero up to 24Gy). The film cut in 2 × 2 cm parts, and put in sterile coverage, then after surgery and placing the applicator, the film parts, puts on interment points. **Result:** We calculated received dose in different organ for 30 patents that this result was obtained:
- Tumor bed mean dose: 14 ± 1.2 Gy
- pectoral muscle dose: 8 ± 0.7 Gy
- skin maximum dose: 1.5 ± 0.3 Gy
- thyroid dose: 0.3± 0.1 Gy
-contralateral breast dose: 0.1±0.04 Gy
Conclusion: Our finding shows that different organ received dose is very less than tolerable maximum dose in one treatment session. This can explain safety of IORT technique in intrabeam system. Also we showed that, EBT3 film in low energy range, is not related to energy or dose rate and using of this film for invivo low energy x-rays dosimetry is very effective.

Intraoperative radiotherapy for breast cancer: A monocentric experience

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PURPOSE: The aim of this work is to compare, in terms of relapse, patients treated with IORT anticipated boost versus patients not treated with IORT but with external beam radiotherapy. For each patient, acute and late cutaneous toxicities have been evaluated using LENT/SOMA classification. Furthermore, a score based on the cosmetic subjective and cosmetic objective outcomes was awarded. **MATERIALS AND METHODS:** From 2012 to date, 76 women (median age 57,8 years – range: 41-80years) with breast cancer were subjected to anticipated boost with IORT followed by a WBI (Whole Breast Irradiation) for a total dose 50 Gy (2Gy/fx). In the same period an equal number of patients with the same neoplastic characteristics was subjected to external beam radiotherapy alone divided into 2 radiotherapy treatment schedules: WBI at 50 Gy (2Gy/fx) plus a sequential boost of 10 Gy (2Gy/fx) or a hypofracionated radiotherapy WBI for a 42.40 Gy (2.65Gy/fx) plus a sequential boost of 10 Gy (2.5Gy/fx). Patients were selected according to the eligibility criteria of an internal protocol resulting from the analysis of national and international guidelines. IORT treatment was performed using a LIAC SORDINA and the prescribed dose was 10 Gy in a single session. The dimension of the applicator was chosen based on the tumor size evaluated exclusively by mammary magnetic resonance. The WBI was delivered by a LINAC-VARIAN equipped with photons of energy of 6-15 MV, the planning technique was 3D conformational through the use of two tangent isocentric shaped fields. The electron energy during IORT treatment, was selected based on the depth of the breast tissue surrounding the resection cavity; the tumor's depth was measured using a millimeter needle inserted several times in the tissue until it touches the radioprotection disc, which according to the manufacturer's instructions has always been inserted and used with a diameter of 2 cm greater than the diameter of the applicator . The electron energy was between 6 and 12 MeV. **RESULTS:** None of patients relapsed in the boost region, only an axillary relapse was diagnosed in 1 patient treated with

IORT. 100% of patients has accumulated a score of E2 in both cosmetic subjective and objective scales. Concerning the LENT/SOMA classification, 19,7 % of patients treated with IORT scored Grade 2, while 2,6% obtained Grade 3 in terms of fibrosis, but all patients are healing within 3 years. **CONCLUSIONS:** IORT is a feasible choice alternatively to external beam radiotherapy in terms of toxicity and cosmetics, furthermore it offers a reduction in the duration of radiotherapy treatment with clear organizational advantages and quality of life for patients. Currently, the role of IORT, in the complementary treatment of breast cancer, is subject to evaluation in many clinical studies and its possible advantages still have to be confirmed, so to clarify and legitimize IORT contribution.

Intraoperative Electron Radiotherapy (IOERT) in breast cancer: We analyze the toxicity and efficacy results in our institution.

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Objetive: Intraoperative electron radiotherapy (IOERT) can be applied during breast conserving surgery to treat invasive breast cancer. We analyze the toxicity and efficacy results in our center. **Material and methods:** Between July 2013 and December 2017, 103 patients with breast cancer were selected for conservative surgery and IOERT in our institution. A total of 104 IOERT treatments were performed (one patient underwent bilateral treatment). One patient performed palliative IOERT, so he was excluded from the analysis. In 62 cases (59.6%) IOERT was administred as a Partial Breast Irradiation (PBI), and in 42 cases (40.3%) due to histopathological characteristics IOERT was administred as a boost (Only 3 patients converted from IOERT exclusive to IOERT boost). The indications for exclusive IOERT were age >60 years, tumor ≤20 mm, negative margins (≥2 mm), Histological Grade I-II, CDI, mucinous, tubular, medullary or colloid, unifocal, unicentric, ER +, c-erb-B2 (-), pN0. Eligibility for boost was: age < 60 o >60 with high risc factor. **Results**: We analized 104 cases. Mean follow-up was 29.8 months (range 1-60). In exclusive IOERT: Median age at diagnosis: 74 years old. Tumour subtype: CDI in 52 cases (83.8%), CLI in 6 (9.6%), CDIS in 3 (4.8%), mucinous in 1 (1.6%). Tumour grade: G1 in 29 cases (46.7%), G2 in 30 cases (48.3%), G3 in 3 cases (4.8%). pT (mm): mean 12.6, range 6-25. ER (+) in 62 cases (100%), 59 patients (95.1%) were c-erb-B2 (-). In boost IORT: Median age at diagnosis: 66 years old. Tumour subtype: CDI in 39 cases (92.8%), CLI in 2 (4.7%), CDIS in 1 (1.6%). Tumour grade: G1 in 9 (21.4%), G2 in 22 (52.3%), G3 in 11 cases (26.1%). pT (mm): mean 17 (range 6-52). ER (+) in 29 cases (69.0%), 32 cases (76.1%) were c-erb-B2 (-). In 100% of the patients, conservative surgery was performed. One patient with margins in contact (performed EBRT), 1 patient with margin less than 0.5mm and the rest of patients presented free margins. Exclusive IOERT was performed in 62 cases (59.6%) with a mean dose 15.5Gy (range 10-20Gy). Boost IOERT was performed in 42 cases (40.3%) with mean dose 10.9Gy (range 10-20Gy) plus External Beam Radiotherapy (EBRT), range: 39-50Gy. Median IOERT energy was 6MeV. Median applicators diameter was 5cm. Median disk diameter was 6cm. In 7 patients (6.7%) skin toxicity grade I-II was evidenced (2 cases after IORT exclusive and 5 cases after IORT+EBRT). The esthetic result was good in 98 patients (93.3%). One patient (0.9%) had local and distant recurrence and 4 patients (3.8%) had distant recurrence with correct local control, to the date two alive and three dead. **Conclusions:** In our experience, IOERT is feasible, efficient, well tolerated and seemed to be beneficial for selected patient. Further follow up will be needed.

Experience of intraoperative radiotherapy (IORT) in an oncological institute of Peru: National Institute of Neoplastic Diseases (INEN) 2014 - 2018

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Introduction: Radiotherapy is an essential part of multidisciplinary treatment in breast cancer, partial irradiation of the breast is one of the techniques used, which aims to achieve greater and effective doses of radiation in the surgical bed (place of greatest risk of recurrence) achieving at least the same adverse effects. These techniques include intraoperative radiotherapy (IOR), which applied alone or as reinforcement (Targit A or Targit B), depending on the pathological risk of the patient, has shown equal effectiveness as conventional radiation but with better cosmetic results, lower costs and better life quality.**Objectives:** To evaluate the effectiveness of the IORT in the management of breast cancer as a sole treatment or as a reinforcement, to describe the viability of the process and the INEN experience in reference to this new treatment. **Material and methods:** We evaluated 216 patients with the diagnosis of breast cancer, who had undergone conservation surgery and received intraoperative radiotherapy between April 2014 and January 2018. Four were excluded, since after the surgery, they underwent mastectomy. **Results:** Of the 216 patients, 69 received IORT as a single treatment (Targit A) and 147 patients as Boost (Targit B). The average age was 58.7 years for patients classified as Targit A (36 - 81 years) and 52.9 years for those of Targit B (27 - 85 years). We defined three large groups, patients with carcinoma in situ, early breast cancer and patients with locally advanced breast cancer who received neoadjuvant initiation. During the surgical act, the time added to the surgery considered as the average irradiation time was 234 minutes [11-48]. The most commonly used spherical applicator was 3 and 3.5 cm in diameter (26.4% and 29.2%). 158 tumorectomies, 32 oncoplastic surgeries and 26 margin extensions (post pathology) were performed. The total number of recurrences observed to date has been four, three of which have been reported in patients with carcinoma in situ who did not receive external radiotherapy and one post-neoadjuvant case who received complementary external radiotherapy. There were no recurrences in patients with infiltrating carcinoma chosen for Targit A. **Conclusions:** The IORT as a single treatment and as a reinforcement associated with external radiotherapy is a viable treatment option in selected patients with breast cancer, which allows us to reduce the time of incorporation into the patient's daily life and therefore improves their quality of life. It also relieves health systems and improves times regarding the comprehensive management of breast cancer. Although we have observed four recurrences in our casuistry, three of them have been presented in patients with ductal carcinom.

First Case Report of the Use of the da Vinci Robotic System as an Assistant in Intraoperative High Dose Rate Remote Brachytherapy (IOHDR).

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Objective: Determine if the daVinci Robotic System was Useful for IOHDR.**Materials and Methods:** In 2014, a 64 year old woman was diagnosed with urethral adenocarcinoma invading the anterior mid-vagina. She underwent pelvic exenteration . Surgical pathology revealed pT3N0 moderately differentiated adenocarcinoma with negative margins. In F2015, she was found to have a right upper lung metastatic lesion treated with wedge resection in February, 2015. She was then started on platinum-based chemotherapy for several cycles. In July , 2015 she was switched to Nivolumab. She remained without progression while on Nivolumab. In 2016, she had to discontinue the Nivolumab due to pneumonitis. She continued to remain off systematic therapies until October, 2017 when a re-staging CT and MRI showed a 3-cm mass in the pelvic floor along the right peri-urtheral vaginal area concerning for recurrence. The mass was just anterior to the vaginal remnant and posterior to the pubic bone . Tumor mass was immediately adjacent to the small bowel and thus SBRT was not feasible. Thus, the patient decided to proceed with surgery and Intraoperative High Dose Rate Remote Brachytherapy (IOHDR). After robotic gross tumor resection, the area of risk involved approximately

3/4th the circumference of the pubic symphysis arch. Two layers of 1.65 mm of lead was placed thru the vaginal opening. The surgeon positioned the lead over the left bowel with the robotic arms. The 3.5 cm cylinder was placed thru the vaginal remnant opening . A cerrobend shield was placed in the left lower quadrant of the cylinder. The tandem was then inserted into the cylinder and the transfer cable was connected to the tandem. The HDR was then programmed to deliver 7.5 Gy at 0.5 cm depth to the proximal 4 cm of the cylinder. The final pathology report revealed a 2.4 cm infiltrating moderately differentiated adenocarcinoma involving the vaginal wall. The patient was simulated post-operatively for external beam radiation to 45 Gy in 25 fractions. **Results:** The intraoperative brachytherapy with robotic guidance was successful in greatly minimizing the dose to the small bowel by robotic retraction of the small bowel and direct visualization / placement of the lead shielding without opening the abdomen or pelvic cavity. The patient has been undergoing postoperative external beam radiotherapy which required a break in treatment after 25.2 Gy due to an ileus. **Conclusion:** The daVinci Robotic System can serve as a Useful Aid in IOHDR.

In vivo Dosimetry of Intraoperative Radiotherapy of breast Cancer by Radiochromic Films with Comparative Dosimetry by Monte Carlo Method.

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Purpose: Intraoperative radiotherapy (IORT) delivers high dose to the tumor cavity in a single fraction. Axxent electronic brachytherapy system (Xoft, Inc., San Jose, CA) is used for breast cancer treatment during surgery in Kaohsiung Municipal Ta-Tung Hospital in Taiwan. The authors verify the depth dose of the Axxent® x-ray source by using Monte Carlo method, and EBT3 radiochromic film. In order to verify the absorbed dose of the breast, we develop an in vivo measurement to identify systematic and random errors in the delivery of treatment. **Material and Method:** Monte Carlo modeling was performed by using Fluktuierende Kaskade (or Fluctuating Cascade, FLUKA) to characterize the Axxent® X-ray source for electronic brachytherapy. GAFChromic EBT-3 films were used for dosimetry. For calibration, films were exposed to radiation produced by Axxent X-ray source using a 35 mm diameter cone. During IORT, the EBT-3 films were wrapped in a thin sterile Tegaderm Film and were positioned on various positions, such as the surface of applicator, under the lead, dissection wound, nipple, the breast edge, and the applicator tube exit. The films were stored for 24 hours and then scanned by an Epson scanner. Results of post-irradiation net optical density were analyzed by the FilmQA pro software. The measurements were determined from absorbed dose to films for the three (red, green, blue) channels in the absorption spectrum. **Result:** 42 patients who underwent IORT were analyzed. The prescribed dose to the applicator surface was 20Gy and the average measured dose was 13.73 Gy. The difference between measured and planned dose was 31.5%. The average dose to under lead was 0.29 Gy.The average dose to skin at the dissection scar was 3.57 Gy, at the nipple was 3.69 Gy, at the breast edge was 0.96 Gy, at the applicator tube exit was 1.68 Gy. The Monte Carlo results agreed with factory measured results to within ±3%. The Monte Carlo results agreed with measured of film results to within ±4%. **Conclusion:** Films calibration has been routinely performed before irradiation. Our results show that EBT-3 films wrapped in sterile Tegaderm Film is a feasible procedure. The measured dose to the applicator was lower than the prescribed 20 Gy. One of the possible reason for the discrepancy was that the position of EBT-3 films had been pushed away from the desired location. It might be due to the balloon size was too small for EBT3 films and thus lead to dosimetry error. These results provide us a real time measurement for IORT and hard evidence for optimizing IORT.

Measurement of peripheral dose to pelvic region during breast intraoperative electron radiation therapy

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OBJECTIVE: This study aimed to measure received dose to pelvic region of patients during breast intraoperative electron radiation therapy (IOERT). Furthermore, we compared the findings with these of external beam radiation therapy. Finally, second ovary and uterus cancer risks following breast IOERT were estimated. **METHODS:** In the current study, the received dose to pelvic surface of 18 female patients during breast IOERT boost were measured by thermoluminescent dosimeter (TLD-100) chips. All patients were treated by a 12 Gy as single fraction. Then, for estimation of the received dose to ovary and uterus of the patients, conversion coefficients of depth to surface dose were obtained in Rando phantom. Given the received dose to pelvic region of the patients, second ovary and uterus cancer risks following breast IOERT were estimated. **RESULTS:** The mean received doses to pelvic surface (ovary and uterus surface) of the patients for 8 and 10 MeV electron beam energies were 9.635 ± 7.286 mGy and 6.873 ± 5.244 mGy, respectively. Corresponding intra-pelvic (ovary and uterus) regional doses were 0.475 ± 0.341 mGy and 0.431 ± 0.331 mGy for 8 and 10 MeV electron beam energies. Findings demonstrated that the ratio of the received dose by pelvic surface to regional dose during breast IOERT was much less than that of external beam radiation therapy. The mean of the second cancer risks for ovary in 8 and 10 MeV electron beam energies were 1.054×10-4 and 1.427×10-4, as well as for uterus were 1.358×10-5 and 6.070×10-6, respectively. **CONCLUSION:** According to our finding, the use of breast IOERT in pregnant patients can be considered as a safe radiotherapeutic technique, because the received dose to fetus was lower than 5 cGy. Furthermore, IOERT can efficiently reduce the unnecessary dose to the pelvis region and lowers the risk of second ovary and uterus cancer following breast irradiation. ADVANCES IN KNOWLEDGE: As an alternative procedure for external beam radiation therapy, the use of IOERT technique in the breast cancer patients can be useful, especially in pregnant patients.

In vivo radiobiological analysis of prostate carcinoma treated with 12 Gy single-shot IORT.

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Purpose: To evaluate apoptotic pathways in prostate cancer treated with intraoperative radiotherapy (IORT), studying the effects on cancer cells, prostatic intraepithelial neoplasia and healthy cells. We evaluated correlations between p53, Bcl2 and ki67, pathological staging and local control. **Material and Methods:** We selected 20 patients. Proteins involved in the apoptotic cascade (Bax, Caspases -3 and -9) were studied before and after 12 Gy in neoplastic tissues, high grade PIN areas and in healthy prostate cells. Immunofluorescent detection of antigens (anti - Bax, anti - caspases - 3 and - 9), were performed on bioptic sample and on surgical specimens 5-mm slices. Before and after IORT, also Bcl2, p53, and ki67 with immunoistochimical analysis were detected. A count of positive spots for immunofluorescence (Bax, Caspases/all nuclei) was performed on tumour cells, PIN and healthy tissue areas. Bax and caspases immunofluorescent positivity was compared in different areas and in neoplastic areas before and after single shot high dose. **Results:** Before IORT, mean Bcl2 in neoplastic cells is 2.23% (range: 1-23), mean ki-67 in neoplastic area is 4.5% (range: 1 -17) and mean p53 is 22.5% (1 - 36). After IORT mean Bcl-2 in neoplastic cells is 8.85% (range: 1 - 28), mean ki-67 in neoplastic area is 7.8% (range: 1 - 18) and mean p53 is 24.9% (1 - 94). A significant increase in Bax expression was detected in tumour and PIN areas comparing treated and untreated samples ($p < 0.05$). After 12 Gy - single dose, healthy areas expressed significantly lower level of Bax positive with respect to neoplastic cells ($p < 0.0001$), while in PIN areas, Bax positive cells were significantly more present than in neoplastic areas ($p = 0.0001$). Results about Caspases 3 and 9 were conflicting and we did not find significant differences in expression between neoplastic and healthy tissue cells after IORT. With multivariate analysis, we find that cancer cells with ki67 ≥ 8% show a trend toward greater expression of Bax ($p = 0.0641$). We do not find correlations between ki67 and caspases activation. We

also found an increasing in Bcl2 expression after IORT in neoplastic areas (p = 0.0041); with multivariate analysis, we found that neoplastic cells with higher Bcl2 expression after IORT had a worsen local control with higher incidence in biochemical failure. Bioptic specimens with p53 higher than 18% and ki67 higher than 8% had worst post-operative staging with higher incidence in extracapsular invasion (p < 0.05) and nodal positivity (p < 0.05). **Conclusion**: After 12 Gy, Bax is overexpressed in tumour and PIN cells. PIN areas seem to be more radiosensitive than neoplastic areas and healthy cells do not activate apoptosis after single dose, showing an intrinsic radioresistance. Pre-operative ki67 and p53 definition could be use in clinical practice to predict patients with worsen pathological stage, while Bcl2 activation after IORT might be predictive factor for failure.

Outcomes and toxicity of electronic superficial Brachytherapy for Non-melanoma Skin cancer in Taiwan

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Introduction: The incidence of non-melanoma skin cancer (NMSC) is high and reaches the 8th rank among all malignancies in Taiwan. Although the mortality of NMSC is low, the incidence keeps on rising. While surgical approaches are the standard treatment, critical lesion sites such as nose, ears, eyelids and lips requires plastic reconstruction with great costs. Instead, a new treatment option for skin cancer is by using Axxent® superficial electronic brachytherapy (EBT) system. The Axxent EBT has surface applicators of four different sizes for delivering 50kV x-ray to the target region.The surface applicator is cone-shaped and also be used as irradiation shield. Therefore, the radiation protection is much easier than systems using radioactive isotopes and thus can be used in most outpatient treatment rooms. The radiation treatment is delivered by hypofractionated course as 8-10 fractions in 4-5 wks, which is far more convenient than the 35 fractions using conventional Linac-based treatment. Besides, the surrounding normal tissue toxicities are reduced due to the nature of brachytherapy. Since NMSC treatment using superficial brachytherapy is very new in Taiwan, we present our experiences (the First in Taiwan) employing Axxent device for cT1-T2 curative treatment. **Material and Methods:** 43 patients with 48 NMSC lesions were treated with EBT to a dose of 40 -50 Gy in eight-ten fractions, delivered twice weekly from June 2015 to December 2018 in Kaohsiung Municipal Ta-Tung Hospital. A commercial head mask fixation device based on thermoplastic materials was used to minimize head movement during radiotherapy. The target lesion depth were evaluated by combined methods of CT images and biopsy. An appropriate size of surface applicator was selected to provide best treatment coverage with acceptable margins. At follow-up, patients were assessed for cosmesis and local control. **Results:** 43 patients (mean age: 74.9years, range: 47-97) with 48 cutaneous malignancies were treated. Tumour reponses and complications were recorded at weekly basis. Most acute reactions were among Grade I-II and all wounds were healed by 6 wks after last treatment session. There has 1patient recurrence to date with a mean followup of 15.4 months (range: 2-31 months). Cosmesis were rated good to excellent for 100% of the lesions at follow-up. **Conclusions:** Treatment of local NMSC with EBT using surface applicators show great effectiveness with low recurrence and favorable cosmetic outcomes. The EBT provides a nonsurgical treatment option for NMSC patients.

Relationship Between Local Recurrence and the Size of Ballon Applicators in Intraoperative Radiotherapy for Early Breast Cancer

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Introduction: Intraoperative radiotherapy (IORT) delivers high dose irradiation to the target region in a single treatment session with equivalent biological effects to 50Gy conventional whole-breast External Beam Radiation Therapy (EBRT). IORT is relatively a new way for breast cancer treatment and is characterized for its time-saving and less toxicity to surrounding tissues. IORT is a form of brachytherapy and requires the cooperation of radiation oncologist and breast surgeon for precise irradiation delivery. IORT for breast cancer treatment has only been employed in recent years in Taiwan and the treatment results are comparable to other published papers. Here, we surveyed the possible reason for local failure by analyzing decisions for the sizes of applicator ballons. **Methods:** From June 2014 to December 2017, 241 patients with early Breast cancer were treated by Xoft® Axxent® system for 20 Gy in one fraction in Kaohsiung Municipal Ta-Tung Hospital. At follow up, patients were assessed for local control. The breast resection volume and balloon volume used in IORT were documented. **Results:** The mean age of the 241 patients was 52.4 years old (range,24-78).117 patient had right side breast cancer and 124 patient had left side breast cancer. There have been 15 loco-regional recurrences and 4 distant metastasis with a mean follow up of 20.8 months (range, 7days–46.4 months). The mean resection volume was 93.455 cm3 and the mean balloon volume was 33.74 cm3. Larger dissection volume didn't necessarily come with a larger ballon and the discrepancy didn't lead to a higher local failure rate ($p>0.05$). **Conclusions:**Treatment of early breast cancer with IORT was effective and the recurrence rate is indifferent from conventional whole breast EBRT. The selection of balloon size should should be based on the resection volume to minimize dead space around the ballon, which could lead to balloon sliding and hence under estimated dosage to the high risk region. Nowadays, systemic treatment such as hormone therapy, chemotherapy or target therapy are often prescribed after surgical resection and radiotherapy and together these might help with local control. Therefore, more cases are still needed for analyzing the influences of ballon sizes in this scenario. With best practices, IORT is a good treatment option for early breast cancer patients.

Investigation of IORT-treated tumor bed modification in breast cancer via inducing biological pathways by new comprehensive approaches; Transcriptomic & Proteomic

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The goal of radiation is to eradicate the remaining microscopic tumor cells. IORT can be applied to deliver irradiation to the cancer site, which delivers electron beams (IOERT) and low kv-x-ray. **Purpose or Objective:** In this study, for the first time and by our knowledge, we decided to investigate the biological effects of IORT in tumor bed of breast cancer in order to confirm the efficacy and beneficiency of IORT. We attempted to answer some clinical/biological questions: "Can IORT (12 and 21 GY) immediately modify tumor microenvironment phenotype by inducing challenges in different cell types with the notion of heterogeneity in tumor margin?" Dose timing can represent powerity of IORT in inducing above changes? Are these changes is related to the received two type of irradiation dose?" **Material and methods:** we used the newest comprehensive techniques in biology; RNA sequencing for transcriptomic study and quantification of proteins by iTRAQ for proteomics study. Six consecutive unselected breast cancer patient entered in our study. All patients were treated with IORT at the time of surgical resection with doses of 12 and 21 Gy and the samples categorized into three groups include: (1) MB; (2) MAi and (3) MA24h. A number of 18 RNA-Seq libraries were sequenced using

Illumina HiSeq™ paired-end sequencing platform and 2X 150bp PE, ~20M Reads; ~6Gb Data for each samples were obtained from individual samples. **Results:** Local pathways such as apoptosis, cell death, DNA damage response, gene silencing, mesenchymal cell apoptosis, phagocytose, positive regulation of cell proliferation, migration, angiogenesis, neutrophil chemotaxis and epigenetics were enriched through IORT in parallel with systemic effects such as; cell metabolism, B-cell receptor signaling pathway and immune responses. All of these biological responses in tumor bed may be towards effectiveness of IORT. **Conclusion:** IORT after tumor excision have ability to use as safe and effective method in tumor margin control and about IOERT with two 12 and 21 Gy , have important local and systemic biological effects on disease control. Duo to IORT effectiveness it may be recommended as a standard method for breast cancer patients.

Investigation of cellular and molecular effects of intra operative X-Ray and Electron beam treated-wound fluid in Breast cancer patient

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Post lumpectomy wound fluid, due to physiologic response to operation and also wound healing process; contains many growth of inflammatory factorsThis stimulatory molecule has pro-tumorigenic potential that could stimulate probably residual tumor cell or cancer stem cell at tumor margin for repopulation, re-newal and recurrence. Tumor microenvironment play an important role in next cell fate decision, to select surviving and proliferation or death/senescence. **Purpose or Objective:** At this study we try to clarify cellular and molecular mechanism of growth arrest or cell death induced by IORT-treated WF and to compare effects of two type of IORT (electron vs photon based X-ray) on four type of breast cell lines. **Material and methods:** Drainage wf over the first 24 h after surgery were collected from each of 15 consecutive unselected breast cancer patient, each group is contained 3 patients, that undergo breast conserving surgery with or without IORT. According to our experiment we used both individual patient samples and pool of all fluids in every group. We used four type breast cell lines then we applied MTT assay for evaluation of proliferation, transwell assay for invasion, PI test for cell cycle, annexin v for apoptosis and ICC for MMP-9 and E-cadherin as tumorigenesis or tumor suppressor molecules. **Results:** our finding showed that proliferation process is not dependent to seroma concentration but over time different cells shows different proliferation response. Also MCF-7 cells had proliferant status particularly after 24L in all groups. In contrary SKBR-3 and MDA-MB-231 cells showed less proliferation response compared with MCF-7. So we can conclude that it is better to be evacuated post lumpectomy seroma in ER+/PR+ breast cancer patient, particularly 24h after operation. By receiving migrasion, invasion and colony assay, we can conclude that electron rays had better inhibitory effects on invasive cell lines, compared to X-Ray. In contrary, WF, wo-TORT attracted the cell to larger extent than the positive control. By reviewing apoptosis and senescence assays WF with and without IORT, has been better effects in inducing cell cycle arrest and death compared to control groups, but no significant difference between type of IORT and among with and wo-IORT group.

Single shot intraoperative radiotherapy for breast cancer, Foligno City Hospital experience

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Purpose: To evaluate local relapse after single shot intraoperative electron radiation therapy (IOERT) for breast cancer. **Materials and Methods:** Between april 2009 and may 2015 58 patients were treated with single shot IOERT at Foligno City Hospital after breast conserving surgery and sentinel node biopsy. Median age was 73 years (range 54-86). Twelve patients (20.7%) were pT1b stage, 37 pT1c (63.8%) and 9 pT2 (15.5%), all patients but 3 had negative sentinel nodes and underwent

axillary dissection with no evidence of further lymph node metastases; in 2 patients sentinel node micrometastases were found but no axillary dissection was performed. Fifty patients had a ductal infiltrating carcinoma, 1 a lobular infiltrating carcinoma, 5 a mucinous infiltrating carcinoma, 1 a tubular infiltrating carcinoma and 1 a low grade ductal carcinoma in situ. Tumor grading was not known in 4 cases (6.9%), G1 in 7 cases (12.1%), G2 in 39 cases (67.2%) and G3 in 8 (13.8%). Three patients were treated for bilateral breast cancer with same histology and stage. All patients were treated with a single shot 21 Gy dose to tumor bed with an electron dedicated machine (LIAC) in the operating room. Energy and reference isodose were chosen after measuring the thickness of the target tissue and ranged from 6 (86.8%) to 8 (13.2%) MeV, reference isodose varied between 85 and 100%. Applicator diameter was chosen after measuring tumor diameter on surgical specimen, a minimum radial margin of 2 cm was given (range 50-80 mm), beveled applicators were not used. In all cases the surgeon positioned a steel/plastic shield between chest wall and target breast tissue. **Results:** Three patients were lost at follow up, the remaining 55 patients had a median follow up time of 70 months (range 9-105). No one developed local recurrence, 8 patients died: 1 of metastatic disease (bones and lungs, no local recurrence), 3 of rectal cancer, 1 of anal cancer, 1 of contralateral metastatic breast cancer, 1 of non-Hodgkin lymphoma and 1 of non oncological disease. **Conclusions:** In selected cases single shot IOERT fo breast cancer is feasible and yields a low percentage of local and distance recurrence.

Comparison between VMAT boost after whole breast irradiation and target as a boost in the management of breast cancer

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Purpose: To compare VMAT boost after whole breast irradiation and TARGIT boost irradiated volumes. **Material and methods:** Targeted Intraoperative Radiotherapy TARGIT was performed, between January 2014 and March 2018, immediately after Breast Conserving Surgery (Lumpectomy and Sentinel Node biopsy and Linfadenectomy if positive sentinel node), using the mobile X-ray system Intrabeam™ wich produces low-energy photons (30- 50 KVp) with a steep dose fall-off in soft-tissue delivering 20 Gy at a radius of 1 mm from the surface, an average of 5 Gy at 10 mm and 1 Gy at 27 mm in about 20 minutes with an spherical applicator of different diameters depending on the size of the lumpectomy cavity. Despite the steep gradient in physical dose, an effective uniform biological dose is distributed inside a rim of about 10 mm around. The EBRT was performed on a LINAC, with conventional fractionation (50Gy in 25 fractions); and hypofractionation (40,05 in 15 fractions, or 42,6Gy in 16 fractions). One houndred and fifteen patients underwent TARGIT at the time of Breast Conserving Surgery and post operative adyuvant Whole Breast irradiation. We compared the boost treatment volumes for EBRT and TARGIT .Primary outcome was the absolute and relative difference between both volumes. For EBRT we delineated the PTV1 and the PTV11 (boost) encompassing the surgical bed, a 10mm expansion to create de CTV and 0,5mm set up margin (PTV). For counturing we used as reference, the planning CT image and the clips in surgical bed. Planning with VMAT was done and the volume encompassing the 95% isodose (V95%) was considered as treatment volume. For the TARGIT, a rim of 1cm around the applicator, encompassing the biological effective dose was considered as treatment volume (V1cm). **Results:** The average V95% in VMAT boost was 168,38cm3 and the median V1cm for TARGIT, 71,58cm3. The median absolute difference between both volumes was 96,80 cm3 that means a decrease in 57% of treatment volume when TARGIT boost was performed. **Conclusions:** TARGIT as a boost allows an optimal localization of surgical bed with a decrease of the irradiated area.

Frequency of whole breast irradiation (WBRT) after intraoperative radiotherapy (IORT)

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Introduction: Accelerated partial breast irradiation (APBI) using intraoperative photon radiotherapy (IORT) has proven to be an effective and safe alternative to whole breast radiation therapy (WBRT) in selected patients. However, some patients are later recommended WBRT after IORT due to surgical pathologic findings, in which case the IORT remains as a boost on the tumor bed. **Objective:** To estimate the rate of WBRT after IORT with our exhaustive diagnostic-therapeutic protocol, that includes pre-operative magnetic resonance imaging, and to make a comparison with the main published series to the purpose of resource planning. **Patients and methods**: From June-2017 to March-2018, the first 52 patients treated with IORT with Intrabeam® were analyzed. The inclusion criteria were based on the consensus recommendations for APBI ASTRO 2016 ,including patients at low risk of local relapse: candidates for conservative surgery, >50 years, infiltrating ductal carcinoma, mucinous, tubular or colloidal ≤2 cm, hormone-dependent and no axillary involvement. **Results**: Among the 52 patients, one did not receive IORT due to the size of the surgical cavity. In 21 patients (41.2%), it was necessary WBRT: 62% nodal involvement, 14% extensive intraductal component, 14% no sentinel node, 5% infiltrating lobular carcinoma, 5% affected margin and one patient with pT>2cm, G3, high risk luminal B. In the TARGIT-A study in the prepathology stratum 21.6% received WBRT. The TARGIT-A trial protocol provided recommendations for WBRT after IORT; however, sites were allowed to customize eligibility criteria. Therefore, we exclude this trial as a reference rate. In the published series by West Pomeranian Cancer Center (Poland), which criteria are based on the APBI ASTRO and ESTRO recommendations, receiving WBRT 51.2% of the patients. In The Breast Centre at the Geneva University Hospital, IORT was given as exclusive radiation therapy in 65% of the patients, whereas 35% received an additional hypofractionated WBRT and the criteria for IORT were adapted from the 2009 APBI GEC-ESTRO recommendations. Unlike our center, WBRT is not recommended for pN1mi by axillary dissection. Another unpublished series (Rodriguez-Ibarría, 2017), which includes 131 patients from the three hospitals in Gran Canaria (Spain), shows that 43.5% of patients received WBRT after IORT. **Conclusion**: The rate of WBRT after RIO is high, from 35 to 51.2%, mainly due to axillary involvement. Our Centre WBRT rate is among those described in the literature. An exhaustive protocol of patient selection for IORT does not reduce it. This data must be considered for the planning of the irradiation resources. It is necessary to unify criteria to associate WBRT after IORT.

Institutional Evaluation on the Use of Intraoperative Radiotherapy in Gynecological Cancers

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Purpose: The radiotherapy options available to patients with locally advanced recurrent gynecologic tumors can be limited due to prior external beam radiotherapy. Intraoperative radiotherapy (IORT) is increasingly utilized to improve outcomes in high risk cases where there is significant concern for local recurrence. We sought to evaluate the outcomes of IORT for recurrent gynecologic cancer from our institution. **Methods:** We performed a retrospective review of all patients treated with IORT in the abdomen or pelvis with a gynecological malignancy from 2009-2016. All patients were treated using the Intrabeam Photon Radiosurgery System. Patient demographics, clinical/pathologic factors, and treatment modalities were analyzed with respect to outcomes including overall survival (OS) and progression-free survival (PFS) as well as toxicities after IORT. Univariate and multivariate Cox proportional hazard ratios and Kaplan-Meier estimates were utilized for analysis. **Results:** We identified 14 patients who underwent abdominopelvic IORT at our institution with a gynecological primary. Median age was 59 (33-86), median follow-up after IORT was 89 mos (25-407), 10 received

prior RT, and 7 had positive margins prior to IORT. Median tumor size prior to treatment was 3.0 cm (2-13) and IORT dose was 1600 cGy (1433-2377 cGy) normalized to the surface. Two patients had cervical cancer, 5 had endometrial adenocarcinoma, 1 had endometrial stromal sarcoma, 1 had fallopian tube serous ACA, and 4 had vulvar squamous cell carcinoma. Ten patients ultimately developed local or regional recurrence after IORT and two developed metastatic disease. There were 7 reports of associated toxicity after treatment including one with anastomotic leak, two with lymphedema, one required surgical debridement, 2 developed neuropathy, and one developed radiation necrosis. One year and 5-year local control rates were 91% and 50%, respectively. One year and 5-year overall survival rates were 91% and 50%, respectively. No variables were associated with local recurrence or overall survival. **Conclusion:** IORT remains a useful technique available in the treatment of recurrent gynecological malignancies. We found that the local control with IORT was excellent and the survival after IORT was also favorable. The toxicities remain minimal even when the majority of our patients had received prior radiation therapy. We did not find a relationship between margin status or histology on local control in this small cohort. Additional multi-institutional research is required to further elucidate the role of IORT especially in the setting margin positive resection.