Head & Neck Cancer

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Modus Operandi

The head & neck multidisciplinary working group meets each Wednesday, to discuss each patient referred to IEO with a cancer of the oral cavity, pharynx, larynx, salivary glands and thyroid for plannnig therapy, evaluating treatment outcome, and scheduling follow-up. On Tuesday afternoon the Thyroid multidisciplinary team meets to evaluate thyroid cancer patients, to plan clinical research activities, and refers results of this discussion during the Wednesday meetings. The last Wednesday of each month the Head & Neck Task Force discusses new protocols, reviews on-going trials, diagnostic and therapeutic guidelines.
Every third month an invited Visiting Professor will attend the department, meet the staff and give a lecture.

Endoscopic CO_2 Laser Surgery for glottis cancer recurrences after radiotherapy.

In this retrospective study the effectiveness of endoscopic laser surgery (ELS) was evaluated in term of local control, organ preservation and complications in 37 consecutive patients (33 men, 4 women) treated for recurrent glottic cancer after radiotherapy. Selection criteria were rcTis, rcT1, or rcT2 with subglottic/supraglottic involvement <5mm and no arytenoid invasion; adequate laryngeal exposure; no previous open surgery; no contraindications to general anesthesia; and signed consent. Median follow up was 44 months (18-88). Thirteen (35%) patients developed a new recurrence: 11 treated by total laryngectomy, 1 supra-cricoid laryngectomy and 1 chemotherapy. Three patients died of laryngeal cancer, one is alive with disease and 1 died of second cancer. Five-year actuarial recurrence-free and overall survival were 57.9% and 86% respectively. The larynx was preserved in 26 (70%). Laryngeal stenosis was the commonest major complication (3/4 women, and 1/33 men). Second primaries occurred in 5 patients. ELS is a safe and effective salvage procedure in selected cases with glottic recurrence after radiotherapy. Oncological results are satisfactory, and organ preservation can be achieved in a high proportion of cases, however the risk of laryngeal stenosis is high in women.

Ansarin M, Planicka M, Rotundo S, Santoro L, Zurlo V, Maffini M, Alterio D, Cattaneo A, Chiesa F. Endoscopic Carbon dioxide Laser surgery for glottic cancer recurrence after radiotherapy: oncological results. Arch Otolaryngol Head Neck Surg 2007, 133: 1193-7.

Prevalence of sublevel IIb metastases

This prospective multicentric study involved the IEO Head and Neck Department, the ENT Clinic of the Brescia University and the ENT Department of Regina Elena Institute in Rome. The objective was to evaluate the prevalence of sublevel IIb lymph node metastases for head and neck primary tumours in 297 patients referred to the above Institutes. All patients underwent neck dissection and sublevel IIb was selectively dissected at the beginning of operation and processed independently. From this study emerges that sublevel IIb dissection is strongly recommended for all patients with cN1 tumors and in those affected by cancer of the parotid gland, skin, and scalp scheduled for elective neck dissection, while this sublevel could be preserved in patients affected by laryngeal cN0 cancer achieving a better functional outcome and the same oncological results than dissection.

Villaret AB, Piazza C, Peretti G, Calabrese L, Ansarin M, Chiesa F, Pellini R, Spriano G, Nicolai P. Multicentric prospective study on the prevalence of sublevel IIb metastases in head and neck cancer Arch Otolaryngol Head Neck Surg 2007; 133: 897-903.

Ultrasound-guided transcutaneous Tru-Cut biopsy in pharyngo-laryngeal masses.

This was a prospective non randomized study. Patients with bulky laryngopharyngeal masses and contraindication to general anaesthesia present diagnostic problems and often should undergo a tracheostomy because of intubation difficulties. In these cases a transcutaneous laryngeal tru-cut US guided biopsy could achieve histological diagnosis sparing tracheostomy. Ten patients entered the study: the procedure was well tolerated and in 9/10 patients the procedure was diagnostic also in patients with a local recurrence after radiotherapy. This procedure is safe and costless and is now largely employed at IEO in patients contraindicated for general anaesthesia or at risk of tracheostomy.

Ansarin M, De Fiori E, Preda L, Maffini F, Bruschini R, Calabrese L, Jereczek-Fossa BA, Chiesa F and Bellomi M. Ultrasound-guided transcutaneous tru-cut biopsy to diagnose endolaryngeal masses. Cancer 2007; 109: 2268-2272.

Mandible reconstruction with autogenous frozen bone.

Mandible symphyseal resection requires composite reconstructions, often with unsatisfactory morphofunctional results. Seven patients with advanced cancer of the foor of the mouth underwent en block resection with immediate reconstruction using the removed mandible treated with liquid nitrogen and covered with a fee forearm flap. In all cases, the resection was radical and no major postoperative complications occurred. Two patients died in 6 months for distant metastases and regional recurrences, in the other 5 patients no local recurrence occurred at a mean follow up of 52 months, but 4/5 had late complications requiring removal of the transplanted mandible. Because of this further clinical and experimental studies are necessary for reduding late complications.

Calabrese L, Garusi C, Giugliano G, Ansarin M, Bruschini R, Chiesa F. Composite reconstruction in advanced cancer of the mouth floor: autogenous frozen-thawed mandibular bone and free-flaps. Microsurg 2007; 27: 21-6.

Pregnancy and thyroid cancer

Thyroid cancer is the most common endocrine malignancy. More frequently diagnosed in women, it is a disease often detected in young patients. About 10% of thyroid cancers occurring during the reproductive years are diagnosed during pregnancy or in the early post-partum period.
Thyroid cancer in young people has generally an excellent prognosis, and survival is similar in pregnant women with thyroid cancer. Thyroid cancer during pregnancy causes considerable anxiety about the optimal timing of recommended treatments and about both maternal and neonatal morbidity.
Pregnancy faced after carcinoma of the thyroid gland obviously needs both maternal and fetal controls to reach an adequate hormonal balance, and to perform safe follow-up controls for the mother and plan further therapy when needed.
Twenty consecutive pregnant women under l-T4 treatment for previously treated thyroid cancer underwent 30 pregnancies from 1994 to 2005 at the IEO. They underwent clinical evaluation and monthly laboratory tests. Gestational data and outcomes were recorded. Fetal growth and thyroid development were checked with a monthly ultrasound evaluation.
In our small group of patients, the antero-posterior diameter of fetal thyroid lies perfectly within the normal or upper range of the control curve, even in patients treated with TSH-suppressive dosages of l-T4. Some of our patients underwent miscarriages, still in normal percentage according to non-treated pregnancies. We recorded chromosomal abnormalities, though in one single patient who had not been previously treated with radioiodine.
In conclusion we could say that pregnancy does not seem to be compromised by thyroid cancer.
Survival and disease-free interval seem identical in pregnant and non-pregnant women, but monthly adjustament of levothyroxine therapy is of the greatest importance for both maternal and fetal well-being.

Gibelli B, Zamperini P, Tradati N. Pregnancy and thyroid cancer. Recent Results Cancer Res 2008; 178: 123-35

On going clinical researches

Mini-invasive surgery and chemo-laser surgery in early laryngeal cancers. The Division goes on with the program of mini-invasive surgery in larynx and thyroid. This includes laser endoscopic cordectomies and supraglottic laryngectomies, and percu-twist tracheotomy in major head and neck surgery. Results of this surgical approach will be published soon.
We started a clinical study on patients with a cT2 glottic cancer. They will undergo preoperative chemotherapy and a subsequent endoscopic laser surgery. Up to March 2008, 30 patients were eligible and 24 entered the study. The study will conclude in June 2008 and results, including also the gene profile of these patients, will be available by the end of this year.

Histoscanning in diagnosis of thyroid lump.
By far the most common presentation of thyroid cancer is a solitary nodule, which can be felt on physical exam. Palpable thyroid nodules are found in 4-7 % of the population and approximately 2-5% of solitary thyroid nodules are malignant. The risk of malignancy per nodule is lower when there are multiple. The Ultrasound (US) examination is used to detect thyroid nodules and it cannot always differentiate between benign and malignant lesions. This technique is used even to guide the Fine Needle Aspiration (FNA). Any procedure that could accurately identify thyroid cancer in the apparently non-cancerous thyroid lobe or in lymph nodes of the neck would be of major help in managing thyroid cancer patients.
HistoScanningTM is an innovative computer aided diagnostic (CAD) technology for ultrasound that quantifies changes induced by cancerous tissues in the backscattered ultrasound waves from soft tissues. It is currently investigated in ovarian and prostate cancer and has the ability to differentiate cancer from non cancer tissues .Our purpose is to develop the implementation of the HistoScan-

ning technology in order to improve the clinical management of thyroid cancer ("THS"). Focused on the detection of malignant lesions of the thyroid with maximum ability to distinguish normal gland, benign, inflammatory and cancer lesions and characterize cancer and non cancer tissue and develop imaging techniques for standardizing THS and THS guided biopsies.
THS algorithm will be applied on thyroids of patients planned to undergo thyroidectomy for suspicion of cancer. It differs from the usual diagnostic ultrasound in two ways. First, the data acquired includes radio-frequency (RF) data as well as raw Cine_loop. The RF data are recorded on a Siemens Antares machine that is equipped with Axius device to record RF data. It is these data that are analyzed using the HistoScannig™ algorithms. Second, the capture of the images is achieved by applying a standardized approach.
In addition the algorithm will differentiate between papillary, follicular, medullary and anaplastic thyroid cancer. This will be possible only if a relevant number of these cancer types are available for establishing the corresponding algorithm. Moreover, the background tissue surrounding the foci of cancer is likely to be representative of those patients who do not undergo thyroidectomy. The majority of these patients will have co-existent benign thyroid hyperplasia, adenomas in addition to acute and chronic thyroiditis. Cancer, therefore, will have to be discriminated from a variety of background tissue. The study started in October, 2007, and in March 2008 twenty-five patients with a pre-op diagnosis of papillary carcinoma have been included. This phase of the study will finish by June 2008.

Study of CT perfusion in Oral and oropharyngeal cancers: a possible predictive exam of response to chemotherapy
Assessment of response to induction chemotherapy is critical and a reliable technique able to predict response to such therapy may have a major impact in patient management, since non responder patients could be shifted to alternative treatment, such as concomitant chemo-radiation therapy or surgery, and improductive treatments could be avoided.
Routinely, endoscopic examination and CT or MR imaging is used for treatment monitoring. Endoscopic examination is invasive and operator dependent and may lead to interobserver variation. On the other hand, assessment of tumor volume changes following therapy by CT may serve as non invasive and objective technique for therapy monitoring, since high intra- and inter-observer agreement has been demonstrated in tumor volume measurements by CT, with good correlation with surgical specimen. However, cross sectional imaging techniques provide only morphologic assessment and may not differentiate viable versus necrotic tumor.
Functional imaging techniques using CT perfusion (CTp) is a new tool that enables to monitor treatment effects non-invasively.
CTp is based on the evidence that CT attenuation is linearly related to contrast medium (c.m.) concentration. When c.m. is injected, the first-pass enhancement is due to c.m. in the intravascular space; as its concentration increases, the extravasation through endothelial capillary membranes into extravascular space begins. A phase of equilibrium between the two compartments is, then, obtained and the maximum tissue enhancement is observed, due to the presence of c.m. both in the intra- and extra-vascular spaces. As time progresses, c.m. concentration in the extravascular space becomes higher than in vascular spaces and c.m. returns to the bloodstream by a passive process. The CTp software use a hybrid model for assessing the distribution of contrast medium in tumor, including a distributed model (in which contrast medium concentration is nonuniform) for the intravascular space and a compartmental model (in which contrast medium concentration is uniform) for the extravascular space. This hybrid model allows the simultaneous determination of the blood flow (BF), blood volume (BV) and blood mean transit time (MTT) in the intravascular space, which are calculated on the first-pass enhancement of c.m., and capillary permeability–surface area product (PS), reflecting distribution of c.m. in the extravascular space, which occurs in the later phase.
We designed a prospective study with the aim first, to assess potential of CTp for monitoring induction chemotherapy in patients with SCCA of upper aerodigestive tract, correlating changes in tumor perfusion following therapy with changes of tumor volume measured on CT, and, second, to assess whether baseline tumor perfusion may predict response to therapy.
Fifteen consecutive patients with locally advanced (stage III or IV) and histopathologically confirmed SCCA of upper aerodigestive tract (oral cavity, oropharynx, larynx and hypopharynx) undergoing induction chemotherapy were enrolled in the study.
Before initiation of induction chemotherapy (baseline), all patients underwent clinical evaluation by endoscopy and, within one week, CT of the head and neck and CTp of the tumor. All patients underwent induction chemotherapy with the following protocol: Cisplatin (100 mg/m^2 intravenously) on day 1, 5-Fluorouracil (1000 mg/m2/die intravenously daily) from day 1 to 5, repeated at 3 weeks interval. After two cycles, a second clinical evaluation by endoscopy was performed. Patients with resectable tumor underwent third cycle of induction chemotherapy, if they had partial or complete response (PR or CR), and surgery or chemoradiation therapy if they had stable or progressive disease (SD or PD). Patients with not resectable tumor underwent third cycle of induction chemotherapy, if they had PR or CR, and

chemoradiation therapy if they had SD or PD.
Patients who completed third cycle of induction chemotherapy, underwent third clinical evaluation and, within one week, follow-up CT of the head and neck and CTp.
In all patients examined, BF, BV and PS of tumor were significantly higher ($p<.05$) in tumor than normal tissue; BF and BV decrease following therapy significantly correlated with tumor volume reduction (respectively, R=.75 and .74). Trend to correlation was found between baseline tumor BV and tumor volume reduction (R.60).
From these preliminary results, CTp showed potential for monitoring response to induction chemotherapy in patients with SCCA of upper aerodigestive tract; high BV may predict high tumor volume reduction following therapy. These results are going to be published in a paper.
A new phase of this study started in November, 2007. In these patients the CTp is performed after the first cycle of induction chemotherapy and correlated to the clinical outcome in order to evaluate as soon as possible the potential radiosensitivity of the tumour. Up to now 12 patients with advanced oral and oropharyngeal cancer were included in the second phase study.