Biological Imaging in Otorhinolaryngology

Essay

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List of Abbreviations

18F FDG	18 Flouride-flurodeoxyglucose
ADC	Apparent Diffusion Coefficient
AJCC	American Joint Committee on Cancer
BF	Blood Flow
BV	Blood Volume
CECT	Contrast-Enhanced Computed Tomography
Cho/Cr	Choline/Creatine Ratio
CPA	Cerebello- Pontine Angle
CT	Computed Tomography
CUP	Carcinoma of Unknown Primary
CWU	Canal Wall Up
DCE	Dynamic Contrast Enhanced
DWI	Diffusion Weighted Imaging
EP	Echo Planner
fMRI	Functional Magnetic Resonance Imaging
Gd	Gadolinium
GLUT	Glucose Transporters
HNSCC	Head and Neck Squamous Cell Carcinoma
HPV	Human Papilloma Virus
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy

List of Abbreviations

MTT	Mean Transit Time
MVD	Mean Micro vessel Density
NAA/Cr	N-acetyl aspartate / creatine ratio
NHL	Non-Hodgkin lymphoma
NIR	Near-Infrared
NPC	Nasopharyngeal Carcinoma
NPV	Negative Predictive Value
OPSCC	Oropharyngeal Squamous Cell Carcinoma
p16 IHC	p16 Immunohistochemistry
PET	Positron Emission Tomography
PPV	Positive Predictive Value
PS	Permeability Surface
RT	Radio Therapy
SUV	Standardized Uptake Value
TEs	Transition Edge Sensor
TSE	Turbo Spin-Echo
TTP	Time To Peak

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INTRODUCTION

Head and neck radiology has evolved during the century since the discovery of the x ray in 1895 by Wilhelm Conrad Roentgen. In the first few decades, conventional radiography was the diagnostic modality for evaluation of head and neck diseases. Special radiographic projections were designed to demonstrate abnormal processes in the paranasal sinuses, temporal bones, base of the skull, and neck. Linear tomography, introduced in 1932, allowed the acquisition of sections that depicted abnormalities that were not clearly defined at conventional radiography. Linear tomography was further enhanced with the introduction of thin section polytomography, especially of the temporal bone, in 1954. Computed tomography and magnetic resonance imaging improved our diagnostic capabilities by enabling location and characterization of tumors, cysts, and inflammatory processes in the head and neck and aiding in earlier diagnosis and treatment ***(Weber, 2001).***

In the past few decades, as oncologists and oncosurgeons attempt to cure many types of cancers or at least provide patients with a longer disease free life, there has been a spectacular parallel and supportive evolution in imaging technology. Currently, imaging plays a pivotal role in the management of all cancers including those of the head and neck. It is used for screening, for preliminary diagnosis to establish the extent and distribution of disease, for biopsy guidance, staging, prognostication, therapeutic planning, judging response to therapy and restaging. In oncology, the role of imaging is shifting, from merely providing anatomical information to providing insight into tumor biology using techniques such as CT, MRI, perfusion imaging, diffusion MR imaging, PET (Positron Emission Tomography) and optical imaging ***(Purandare et al., 2010).***

18 Flouride-flurodeoxyglucose (18F-FDG) PET has - in the last few years- become an established modality in the management of several cancers. It is an imaging technique that provides information about the metabolic changes associated with cancer. PET scanning requires the use of molecules that are labelled with radio nuclides. Numerous such positron emitting radio-isotopes exist and are used in clinical experiments and research. However in clinical PET practice the principal radio-isotope used is the positron emitting 18F-FDG which is a glucose analogue labelled with 18F ***(Purandare et al., 2010).***

PET/CT is strongly applied in the head and neck malignancies, the most common of which are squamous cell carcinoma of the upper aero-digestive tract, salivary and thyroid glands malignancies in addition to lymphomatous deposits. It can be added to the work up of carcinoma of unknown origin or to guide biopsies. Furthermore, PET/CT potentially supports tumor volume delineation in radiation therapy planning in the head and neck where a multitude of sensitive structures is confined to a small area of the body ***(Poeppel et al, 2009).***

Diffusion weighted imaging (DWI) using ***MRI*** is the simplest form of diffusion imaging. DW sequences are sensitized to detect the Brownian (random) motion of water protons in biological tissues. The apparent diffusion coefficient (ADC) is a mathematical quantification of the extent of free diffusivity of water molecules. The intrinsicT2 signal changes contributing in the diffusion images are eliminated in ADC maps. In normal tissues where there is unrestricted motion of water protons no restricted diffusion

can be measured. However in tumors with high cellularity there is restricted diffusion of water protons which can be measured quantitatively. This technique is being extensively used in brain for diagnosing acute infarcts and for differentiating high grade tumors (that display restricted diffusion) from low grade ones ***(Purandare et al., 2010).***

Extracranial applications of diffusion-weighted (DW) magnetic resonance (MR) imaging are gaining increasing importance. Currently, DW imaging is being evaluated for several cancers of the body, as well as for assessment of function in organs such as the kidneys, pancreas, and salivary glands and in head and neck radiology. The main indications for performing DW imaging in head and neck- the relatively small but challenging region of the body- are tissue characterization, nodal staging, therapy monitoring, and early detection of treatment failure by differentiating recurrence from post therapeutic changes ***(Thoeny et al., 2012).***

Perfusion imaging, whether performed with CT or MRI, evaluates dynamic microscopic blood flow changes through a region of interest. Changes in tissue signal intensity (MRI) or attenuation (CT) are measured during a dynamic contrast infusion. Blood flow, blood volume, and transit time parameters of tissue regions can be then generated, either on the CT scanner or on a separate workstation with commercially available software. Perfusion characteristics of tissue demonstrate changes in blood flow or volume of the interrogated areas depending on the underlying pathologic processes ***(Shah et al., 2008).***

An additional area of interest is in regard to tumor recurrence or regression. As conventional MRI or CT may simply demonstrate increased contrast enhancement within the treated neck. Morphologic changes in tissue appearance (such as increase in size or nodularity) may not be well demonstrated on early post-treatment conventional imaging. However, recent studies have concluded that for recurrent oral cavity and oropharyngeal carcinomas, perfusion parameters are altered. Specifically, blood volume and blood flow within recurrent tumor tissue are elevated in comparison to therapy-altered tissue, with corresponding decreases in transit time ***(Bisdas et al., 2007).***

Optical molecular imaging: For cancer surgery with curative intentions, radical resection i.e., (removal of all cancer cells) is a sine qua non. To achieve this, the surgeon has to adequately assess the tumor resection margin during the operation. Optical molecular imaging using near-infrared (NIR) fluorescence introduces a revolutionary new approach to address this basic challenge in surgical oncology ***(Keereweer et al., 2013).***

Preclinically, optical imaging has been used in tumor identification, image guided resection, therapy monitoring, and detection of sentinel lymph nodes. Because tumor specific agents were not yet approved for clinical use, the first clinical studies were conducted using nonspecific fluorescent agents that had long been approved for different applications and could therefore be used for sentinel lymph node mapping ***(Mieog et al., 2011).***

Chapter I

PET/CT scan

Introduction

Positron emission tomography (PET) is a molecular imaging technique in which positron-emitting radionuclide tagged tracer molecules are used to trace a biologic function within the body. It can provide valuable information about different pathologic as well as physiologic processes, depending on the type of used radiotracer ***(Rohren et al., 2004).***

The major clinical application of PET is in oncology, using 18F labeled fluorodeoxyglucose (18F-FDG). By this way, it gives quantitative and qualitative functional information about tumor cells depending on their increased rate of glucose metabolism. 18F-FDG PET is regarded to be effective in detection, staging and restaging of malignancies with a remarkable high sensitivity. Its major limitations have been the lack of anatomical landmarks, relatively blurred images and limited spatial resolution ***(Rohren et al., 2004).***

In the last decade, the ***combination of PET and computed tomography (PET/CT)*** has been introduced in the field of oncologic imaging. Combined PET/CT represents a very unique imaging modality that scans the whole body in the same session, providing functional and anatomic information in co-registered images. It combines the high sensitivity of PET to the superior anatomical localization by CT resulting in

much more accurate detection and staging of malignancies. It also provides a better quality PET images due to better attenuation correction by CT scan in a relatively short time ***(Von Schulthess et al., 2006).***

Accordingly 18F- FDG PET/CT has acquired a firm place in the evaluation of malignancies. It is rapidly becoming the key investigative tool for the loco-regional staging and detection of distant metastases. It has a quite greater role in assessment of recurrence and differentiating it from post therapeutic tissue changes. It has also gained widespread acceptance as a key tool used to demonstrate early response to therapy before other markers of response. PET/CT impacts the patient's prognosis by altering the management strategy according to the obtained findings during the initial staging or the follow up (during the course of treatment or later follow up) ***(Ben-Haim and Ell., 2009).***

PET/CT is strongly applied in the head and neck malignancies, the most common of which are squamous cell carcinoma of the upper aero-digestive tract, salivary and thyroid glands malignancies in addition to lymphomatous deposits. It can be added to the work up of carcinoma of unknown origin or to guide biopsies. Furthermore, PET/CT potentially supports tumor volume delineation in radiation therapy planning in the head and neck where a multitude of sensitive structures is confined to a small area of the body ***(Poeppel et al., 2009).***