

Review

Imaging modalities in head and neck cancer patients- overview

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Accepted 27 February 2011

Accurate staging and timely assessment in head and neck cancer patients is critical for initiating appropriate treatment strategy. Therefore, pre-treatment imaging in diagnosis is of great importance. Computerized tomography, introduced in the early 70s, followed by magnetic resonance imaging, positron emission tomography, refinements in ultrasonography, and advances in nuclear medicine and applications such as sentinel node lympho-scintigraphy have greatly added to diagnostic accuracy. Post-treatment CT or MRI is of value when a recurrent tumor is suspected, to confirm the presence of such a lesion and to determine its extent; this is important information for determining the possibility of salvage therapy.

Key words: Positron emission tomography, magnetic resonance imaging, computed tomography, sentinel lymph node scintigraphy, multi-detector row CT.

INTRODUCTION

The last 30 years have seen an increase in knowledge on technical advances in the diagnosis of oral cancer (major advances in the knowledge and understanding of the epidemiology, aetiopathogenesis, diagnosis, management and prognosis of oral cancer, 2009). Accurate staging at presentation of patients with head and neck squamous cell carcinoma (HNSCC) is critical for treatment selection: delineation of the primary tumor, assessment of the presence and extent of lymph node metastases and screening for distant metastases (Remco de Bree, 2009). Computerized tomography, introduced in the early 70s followed by magnetic resonance imaging, positron emission tomography, refinement in

ultrasonography and advances in nuclear medicine and applications such as sentinel node lymphoscintigraphy have greatly added to diagnostic accuracy. It is important to determine the right indications for these new diagnostic techniques. The merit and demerit of the different image modalities are shown in Table 1.

PRIMARY TUMOR

The most important information required before treatment for proper therapeutic planning is accurate knowledge of location, size, extent and depth of invasion of a primary tumor and its relation to the surrounding structures (Remco de Bree, 2009). Sensitivity of FDG-PET (F-18-fluoro-deoxyglucose –positron emission tomography) is reported to be 98% and that of FDG-PET-CT 97% for the detection of primary tumors in patients who had newly diagnosed HNSCC. PET alone cannot delineate the extent of tumor (Roh et al., 2007). Since physical examination usually shows the primary tumor, the role of FDG-PET is limited to the detection of the occult primary tumors in patients with cervical lymph node metastases in

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Abbreviations: CT, Computerized tomography; MRI, magnetic resonance imaging; HNSCC, head and neck squamous cell carcinoma; FDG-PET, F-18-fluoro-deoxyglucose-positron emission tomography; US, ultrasound.

Table 1. Merits and demerits of different imaging modalities

Imaging modality (Remco de Bree, 2009; Bondt et al., 2007; Shah et al., 2003)	Merits	Demerits
Ultrasonography	<ol style="list-style-type: none"> 1. Low cost 2. No ionizing radiation 3. With guided fine needle aspiration it is the accurate method to evaluate neck lymph node 4. Used for detection of superficial masses in children 	<ol style="list-style-type: none"> 1. Operator dependent 2. Time consuming
Computed tomography	<ol style="list-style-type: none"> 1. For pre and post treatment imaging 2. Highly sensitive for extra capsular spread of tumor 	<ol style="list-style-type: none"> 1. Does not differentiate reactively enlarged lymph node from metastatic lymphadenopathy
Magnetic resonance imaging	<ol style="list-style-type: none"> 1. Tumor extent can be better defined along with contrast agent. 2. Detect metastatic neck adenopathies. 3. Better tumor perfusion detection by dynamic contrast enhanced MRI than CT. 4. DWMRI provides information about microscopic structures such as cell density, cell integrity and vascularity. 	<ol style="list-style-type: none"> 1. Not reliable to detect small tumor deposit with in non-enlarged lymph node 2. Per treatment tumor volume appear significantly smaller than CT.
FDG-PET	<ol style="list-style-type: none"> 1. Most frequently tracer to reflect the metabolic activity of tumor volume 2. Highly reliable after 3 to 4 months of end of treatment 	<ol style="list-style-type: none"> 1. High cost 2. Limited to the detection of occult primary tumor in cervical lymph node metastasis in the neck. 3. Unreliable if done early after the end of treatment. 4. Automatic segmentation of tumor volume is not possible due to increase in background signal by radiation induced inflammation
PET-CT	<ol style="list-style-type: none"> 1. Best accuracy for detecting occult cervical lymph node metastasis in No neck. 2. Provides help in evaluation of patients with suspected recurrent SCC of head and neck, in whom anatomic imaging is inconclusive due to loco regional distortion. 	<ol style="list-style-type: none"> 1. PET alone cannot delineate the extent of tumor.

**Sensitivity and specificity of imaging modalities in head and neck lymph node staging
(Adams et al., 1998)**

Imaging modality	Sensitivity (%)	Specificity (%)
Ultrasonography	72	75
CT	82	85
MRI	80	79
FDG-PET	90	94

the neck (Remco de Bree, 2009).

Lymph node metastases

Since the status of the cervical lymph nodes is the single most important tumor related prognostic factor, optimal treatment planning requires knowledge of the exact involvement of the neck nodes. Patients with clinically manifest lymph node metastases require some form of techniques, like computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US) and especially US-guided fine needle aspiration cytology are more reliable than palpation (Bondt et al., 2007). It is found in a meta analysis that, FDG-PET has a good performance in the overall pre treatment evaluation of the presence of lymph node metastases in HNSCC patients (Kyrzas et al., 2008). Detection of occult lymph node metastases is the most important prognostic indicator. A meta analysis showed that, FDG-PET detect only 50% of the occult lymph node metastases, reiterating the inability of imaging test to document microscopic disease (Kyrzas et al., 2008). In a study it showed that, for the detection of subclinical lymph node metastases the visual correlation of FDG-PET with CT/MRI has been reported to be more accurate than FDG-PET alone (Ng et al., 2006). Although PET and PET-CT have probably the best accuracy for detecting occult cervical lymph node metastases in the clinical N0 neck, these techniques are still not reliable enough to avoid elective treatment of the neck (Remco de Bree, 2009).

In patients without clinical signs of lymph node involvement, sensitivity of fluoro-2-deoxy-D-glucose PET is only 50%. This has led to the use of sentinel lymph node scintigraphy, that seems to be a valid alternative to elective stage dissection. The sentinel lymph node (SN) concept is fundamentally based on the theory of orderly spread of tumor cells within lymphatic system. The first lymph node in a regional lymphatic basin that receives lymphatic flow from a tumor, is considered to be the SN.

In the SN procedure, this lymph node is identified using radioactive colloid and blue dye. This SN is examined in detail histopathologically, using stepped serial sectioning and by immunohistochemistry. The SN concept assumes that lymphatic metastases are always identified in the SN, so that a tumor –negative SN precludes the presence of lymphatic malignant involvement. The sensitivity of this technique is estimated as 93% (Ng et al., 2006). The SN procedure is less reliable if the (sentinel) lymph node contains a large tumor deposit (Ross et al., 2004).

Therefore, other imaging techniques, such as USgFNAC, are needed to select patients for the SN procedure to avoid false negative findings.

New high-resolution MRI sequences and the

development of specific contrast agents are offering new possibilities in the diagnostic work-up of head and neck lymph nodes. Diffusion weighted MRI uses the apparent diffusion coefficient (ADC) as a marker of cell density. These ADCs are the highest in benign lymphadenopathy and the lowest in metastatic nodes. However, the presence of necrosis in metastatic cancers increases the ADCs of the nodes. Therefore, DW MRI is considered complimentary to standard MRI. Further implementation of DW MRI into routine clinical practice probably will depend on the improved standardization of imaging technique and interpretation (Remco de Bree, 2009).

Detection of distant metastases

The reported incidence of clinically identified distant metastases in HNSCC at presentation varies from 2 to 18% (Bree et al., 2000). This incidence is directly related to the stage of disease, particularly to the presence and extension of lymph node metastases and loco-regional control and depends on the applied diagnostic methods (Bree et al., 2000). FDG-PET is a sensitive whole-body technique which has shown potential for the detection of distant metastases (Brouwer et al., 2006). Most studies that used FDG-PET in screening for distant metastases lack fair and controlled comparison between PET and other standard conventional imaging such as chest CT and/or an adequate gold standard such as reasonable follow up (Senft et al., 2008). FDG-PET had a higher sensitivity and had higher predictive positive value. One concern of using FDG-PET for screening is its cost. On the one hand FDG-PET is an expensive diagnostic technique, but on the other hand detection of distant metastases avoids futile expensive treatment.

FDG-PET lacks precise anatomical resolution and may over diagnose some inflammatory conditions. By virtue of its high spatial resolution, multi-detector row CT (MDCT) may serve as a cross sectional imaging tool complementary to FDG-PET in evaluation of distant metastases in HNSCC patients and help to characterized FDG abnormalities (Remco de Bree, 2009). Combination of PET and CT in PET-CT is an attractive option, potentially combining the best of both worlds, and providing a one-stop shop for the patient. In recent years, dual modality PET-CT has been used to provide accurately fused functional PET and morphological CT in a single examination (Remco de Bree, 2009).

However, in clinical practice the detection of asymptomatic distant metastases during follow-up is of less importance since currently no treatment options with curative intent are available. Unfortunately, comparisons between the accuracy of CT, PET, visual correlation of PET and CT integrate PET-CT were not made. Due to the introduction of multi-receiver channel MR, whole body MRI (WB-MRI) has become clinically feasible, with substantially reduced examination times. WB-MRI shows

potential in detecting metastases of primary head and neck tumors (Ng et al., 2008).

IMAGING DURING (CHEMO) RADIOTHERAPY

Measurable anatomic changes occur during the course of radiotherapy for head and neck cancers, mainly during the second half of the treatment. Such volumetric and geometric changes can have a potential dosimetric impact when conformal treatment techniques are applied. Compared to pre-treatment CT, the per-treatment tumor volume appeared significantly smaller on MRI than on CT. Per-treatment automatic segmentation of tumor volume on FDG-PET is not possible due to tremendous increase in background signal by radiation-induced inflammation (Robert, 2006).

Post treatment imaging

After treatment of a head and neck cancer, a number of tissue changes become visible on CT and MR images of the neck. These expected alterations should be known, so that they are not misinterpreted as evidence of persistent or recurrent tumor. Imaging is of value for surveillance in patients with a high-risk profile for tumor recurrence after treatment and as an adjunct to clinical follow-up. Imaging may be used to monitor tumor response and to try to detect recurrent or persistent disease, before it becomes clinically evident, possibly with a better chance for successful salvage. Some authors recommend FDG-PET for detecting residual nodal disease. However, FDG-PET obtained early after the end of therapy appears to be unreliable (Robert, 2004).

CONCLUSION

Sophisticated imaging methods play an increasingly important role in the management of head and neck cancer. Pretreatment imaging has predictive value for patient outcome, independently from the currently used TNM classification, and may be used to tailor treatment plans. Based on per-treatment imaging, individualized replanning during radiotherapy may ameliorate tumor control rates and reduce toxic effects to normal tissues. Post-treatment CT or MR imaging is of value when a recurrent tumor is suspected, to confirm the presence of such a lesion and to determine its extent. More rarely, imaging may be of use in the differentiation between tumor recurrence and treatment complications.

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