PET/CT IN INITIAL STAGING AND RESPONSE ASSESSMENT OF HEAD AND NECK CANCER.
Προσωπικά ή ως μέλος εργασίας/εργοστήριος ιατρού ή μέλος της εταιρείας μας οπουδήποτε ανακάνετε ή άλλως ακούσατε διαφημίσεις από τις εταιρείες/επιχειρήσεις που διαχειριζότανταν την άνω επίλυση κατά τη διάρκεια των τελευταίων 4 ετών.

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Χαρακτηριστικά:
Anabisia, AstraZeneca, Bristol, GenéricosPharma, Medgenics, Coloplast, Merck Serono, MSD, Novartis, Pfizer, Roche, Sanofi Genzyme, SYN Innovations.

Ό,τι αναφέρετε ή άλλα κάτι άλλο έχετε ισχύσει:
✓ Οποιεσδήποτε παράγοντες που παράβαζαν τη διάρκεια των τελευταίων 4 ετών και ή τη συμπεριφορά / διαχείριση που χρηματοδοτούσαν τη συγκεκριμένη επίλυση, καθώς και:
✓ Οποιεσδήποτε υποθέσεις, συμβάσεις ή διαφωνίες ή άλλες θέσεις τα τελευταία 4 χρόνια ή κίνηση, τις οποίες ουσιαστικά διαχειρίζατε / διερευνάτε που χρηματοδοτούσαν τη συγκεκριμένη επίλυση.

[Signature]
NORMAL UPTAKE

Salivary glands

parotids

tonsils

Brown fat
FDG = HYPERMETABOLISM
INITIAL STAGING
FDG PET/CT usage is constantly increasing in the initial staging of HNC.

Nowadays statistics show that the modality is used in up to the half of patients in initial staging - compared to 10% in 2005.

Guidelines recommend the routine usage in initial staging in patients suspicious for III or IV disease stage.

It can offer valuable information about additional lesions, nodal disease and better delineation of the tumor size and borders.
Tumor size is better estimated (Hideghety et. al. 2015), with up to 86% of the patients having smaller GTV using FDG PET/CT compared with other imaging methods, offering great help to treatment plan.

Method’s sensitivity in lymph node disease is higher than CT for both ipsilateral and contralateral lymph nodes, since the diagnosis is not only based on size and morphology.

PET/MR theoretically has better potentials for lymph node staging. Studies so far do not prove this. (Platzek et. al. 2014).

FDG PET/CT is the ideal imaging modality for distant metastases detection.
Prospective study of 102 HNC patients with histological confirmation.
Comparison to conventional imaging.
Great impact on T,N,M stage.
Increase of T stage in 36 patients and decrease in 10.
N downstaging in 27 patients and increase in 8.
13 patients were moved from M0 to M1 stage.
In summary 9 patients were upstaged and 18 downstaged.
Radiotherapy plan was changed in 14 patients.

Abramyuk A. et al. 2013

Multi-centre study of 223 newly diagnosed patients with HNSCC.
Stage change in 43% of the patients.
In 30% of the cases patients were upstaged.
In 13% there was downstaging.
Treatment plan was changed in 14% of the patients.

Lineux et al. 2011
Hypermetabolic lymph nodes in the left cervical area.
Hypermetabolic lesions at the oropharynx, at the lateral cervical areas and the left supraclavicular area.
There is increasing interest in the prognostic value of markers like SUVmax, TLG, MTV, in the initial staging.

In a more personalized basis, the usage of the metabolic markers can lead to decisions regarding the aggressiveness of treatment.

Increased metabolic markers values are associated with worst prognosis.

SUVmax > 13 is linked to decreased survival (Suzuki et.al. 2013).

SUVmax >8 in SCC of the pharynx is associated with smaller OS (Suzuki et.al. 2014).

SUVmax >10, MTV>20 ml, TLG> 70g could predict the outcome in terms of DSS and DFS (108 pts with HNSCC) (Koyasu et. Al 2014).

In patients with more aggressive characteristics and worst prognosis based on FDG PET/CT criteria, more aggressive decisions can be taken.
2-9% of HNC patients will have as first sign cervical lymphadenopathy.

FDG PET/CT detects primary site at about 25% of the cases (Rusthoven et.al. 2004)

The usefulness of the method is established with central role in the management of the patients.

In a metanalysis of 16 studies (totally 302 patients), sensitivity and specificity is calculated to 88.3 and 75% respectively in CUP patients with cervical metastases. Primary site was discovered in 25% of the patients with negative CI. (Rusthoven et.al. 2005).

In mixed CUP population with cervical and extra-cervical metastases, the percentage of detection of primary site, sensitivity and specificity were respectively 34, 84 and 84% (Kwee and Kwee 2009).

Results are better when PET/CT is performed before panendoscopy (Waltonen et.al. 2009- Johansen et. al. 2011).

The images can also guide the clinician to the better site for biopsy.
Hypermetabolic lesion in the right side of the oropharynx (primary site) and hypermetabolic lymph nodes in the right cervical area (clinical presentation).
One of the main causes of treatment failure.

In a review of 12 studies between 2000 and 2011, the methods sensitivity and specificity is reported over 90%.

The site of the second primary is important: In lesions of the upper gastrointestinal and especially the esophagus the sensitivity is lower.
INITIAL STAGING-SECOND PRIMARY

SECOND PRIMARY-LUNG CANCER
GTV is more precise when bases on FDG PET/CT.

The main contribution is when surroundings tissues are infiltrated, after initial therapy or surgery, in cases that active disease and post treatment changes are difficult to discriminate based on CT.

Also in the case of metal materials that cause artifact the method is very useful.

It can detect more lesions than known, so that they can be included in the treatment plan.
In case of IMRT it can help when the tumor has metabolic heterogeneity.

The method can help the clinician to draw a more personalized treatment plan for the patient.
RESPONSE TREATMENT ASSESSMENT
Study of 28 patients of stage III-IV that underwent FDG PET/CT study before and after ICT, reduction of MTV of 42% or more and TLG of 55% could predict good prognosis (Yu J et. al. 2014).

SUVmax reduction of 65% after ICT (2-4 week), could predict the results of CRT and predict OS (Yoon DH et. al. 2010).

Reduction of SUVmax 1-2 weeks after CRT >50% in the primary tumor was associated with better 2-year survival. (Hentscel et. al. 2011).

In a study (Ceulemans et. al. 2010), it was enquired if FDG PET/CT during therapy could substitute a study after the end of therapy regarding tumor response. The results showed that post therapy study could not be substituted.
The imaging time after therapy is extremely important. Early imaging can lead to increase of false positive results. Increased uptake after therapy can persist up to 16 weeks after therapy. 12 weeks after therapy is an acceptable time interval, especially if the rest of imaging performed earlier is negative. Sensitivity and specificity is higher 10 weeks after CRT compared to earlier studies. (Gupta et. al. 2011). FDG PET/CT studies in patients with locally advanced HNC and imaging performed at 16 week post treatment find NPV of almost 100% (Prestwich et. al. 2012). Studies comparing FDG PET/CT with MRI, show that PET/CT is superior, especially in 3-6 months after treatment, providing more accurate discrimination between viable and non viable tissue. PET/MRI scanners show promising in this field, but studies are limited, especially in the cost-effectiveness area.
In this prospective, randomized, controlled trial, the non-inferiority of positron-emission tomography–computed tomography (PET-CT)–guided surveillance (performed 12 weeks after the end of chemoradiotherapy was assessed, with neck dissection performed only if PET-CT showed an incomplete or equivocal response) to planned neck dissection in patients with stage N2 or N3 disease. The primary end point was overall survival.

564 patients (282 patients in the planned-surgery group and 282 patients in the surveillance group) from 37 centers in the United Kingdom. Among these patients, 17% had nodal stage N2a disease and 61% had stage N2b disease. A total of 84% of the patients had oropharyngeal cancer, and 75% had tumor specimens that stained positive for the p16 protein, an indicator that human papillomavirus had a role in the causation of the cancer. The median follow-up was 36 months. PET-CT–guided surveillance resulted in fewer neck dissections than did planned dissection surgery (54 vs. 221); rates of surgical complications were similar in the two groups (42% and 38%, respectively). The 2-year overall survival rate was 84.9% (95% confidence interval [CI], 80.7 to 89.1) in the surveillance group and 81.5% (95% CI, 76.9 to 86.3) in the planned-surgery group. The hazard ratio for death slightly favored PET-CT–guided surveillance and indicated noninferiority (upper boundary of the 95% CI for the hazard ratio, <1.50; P=0.004). There was no significant difference between the groups with respect to p16 expression. Quality of life was similar in the two groups. PET-CT–guided surveillance, as compared with neck dissection, resulted in savings of £1,492 (approximately $2,190 in U.S. dollars) per person over the duration of the trial.

Survival was similar among patients who underwent PET-CT–guided surveillance and those who underwent planned neck dissection, but surveillance resulted in considerably fewer operations and it was more cost-effective.
Studies enquiring the cost effectiveness of FDG PET/CT in head and neck cancer patients management, show that despite the cost of the study, because of the reduction of unnecessary additional treatments and interventions, there is a cost reduction when the method is used in initial diagnosis.

In an Australian prospective study it was found that the reduction of unnecessary lymph node dissections, lead to a major cost reduction for healthcare system.
CANCER OF THE MOUTH CAVITY BEFORE AND AFTER THERAPY
TONGUE CANCER – RESTAGING

POST RADIATION FINDINGS
OROPHARYNX CANCER RESTAGING
Because of the incidence of false positive findings in the course of the post therapy period, several attempts have been made to increase specificity.

Several cut-off points have been used regarding the SUV\textsubscript{max} of the primary tumor and the lymph nodes.

Tumor activity of 5-6.5 or less and lymph nodes SUV\textsubscript{max} of 2.8-3.2 or less, in several studies could predict therapy response.

The is a lack of a standardized method of response assessment.

In this direction the usage of criteria like Deauville criteria used in lymphoma response assessment was proposed. In Deauville criteria there is a comparison with SUV\textsubscript{max} of the liver and mediastinal blood pool.

With the alteration of using internal jugular vein activity instead of mediastinal blood pool there was the introduction of Hopkins criteria.
Hopkins criteria show satisfying specificity and NPV of 92% and 91.5% respectively.

It’s five scaled, taking into account the diffuse or focal pattern of the uptake.

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<th>GRADE</th>
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<td>1</td>
<td>Complete metabolic response-less uptake than IJV.</td>
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<tr>
<td>2</td>
<td>Likely complete metabolic response: uptake more than IJV but less than liver.</td>
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<tr>
<td>3</td>
<td>Probably post radiation inflammatory changes: Diffusely more than liver.</td>
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<tr>
<td>4</td>
<td>Probably residual tumor: Focal uptake more than liver.</td>
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<td>5</td>
<td>Residual tumor: Intense and focal uptake.</td>
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(Grades 1-3 are considered negative, while grades 4-5 are considered positive for tumor)
TREATMENT RESPONSE CRITERIA

(A) Before treatment
(B) After treatment 1
(C) After treatment 2
(D) After treatment 3
(E) After treatment 4

(A) Before treatment
(B) After treatment 1
(C) After treatment 2
(D) After treatment 3
(E) After treatment 4
FDG PET/CT shows high NPV during follow-up (Paidpaly et. al. 2013, Kim et. al. 2013, Robin et. al 2014, Ho et. al. 2013).

High NPV values around 95%.

Patients with a negative study 4-6 months after therapy are considered of low-risk and could undergo less intense follow-up. (Lee et. al. 2007).

The ones with a positive study are likely to have a worst outcome (Paidpally et. al. 2013, Kim et. al. 2013).

In patients with a clinical suspicion of relapse in HNC a negative study can rule out relapse. (Gao et. al. 2014).

Studies that enquire the value of successive FDG PET/CT studies after a first negative study (Lee et. Al. 2007, Ho et. Al. 2013), show that in low risk patients there is no benefit. High risk patients need a second negative study (2 negative studies in 6 months or a negative study 1 year after). As expected patients with a positive study have a worst outcome.
LARYNX CANCER - FOLLOW UP

Local relapse
Local relapse – distant mets
1. The method offers higher sensitivity and specificity in staging, especially important in stages III and IV.

2. Earlier and more accurate evaluation of therapy effect - keep in mind the period between the end of treatment and imaging.

3. Important prognostic information provided by the technique give the possibility of more personalized treatments with better patient outcome.
FDG PET/CT IN DTC

- FDG PET/CT is not routinely recommended in pre-surgery evaluation of DTC.
- Only per-patient basis in aggressive histology or in cases that distant metastases are suspected the method may have a place.
- The main application is in cases of rising thyreoglobulin and negative whole body imaging with radioiodine. Studies show that management of the patients is altered in up to 50% (Chung et al. 2012). Meta analyses show sensitivity and specificity of 84% (Dong et. Al. 2014).
- In Hurthle cell carcinoma the method has a place in initial staging and follow up with sensitivity and specificity of 95% (Pryma et. Al.)
- The method is also useful in ATC.
- FDG PET/CT has gives also prognostic information. In patients with metastases FDG uptake can recognize patients that are expected to respond poorly to therapy with radioiodine (dedifferentiation).
- In medullary cancer can help in cases of rising of markers after surgery.
- In any FDG PET/CT study random focal uptake in the thyroid (incidentaloma) needs further correlation: There is a possibility of ~30% of cancer.
PAPILLARY THYROID CANCER - RISING THYREOGLOBULIN-NEGATIVE RADIOIODINE.

Hypermetabolic lymph nodes – disease relapse
MEDULLARY CANCER - RISING CALCITONIN

Disease relapse
Οι επιπτώσεις της ραδιενέργειας με τη πάροδο του χρόνου...

Hour:
1  4  6  9
12 14 17 19
21 23 26 29
31 36

[Diagram showing smiley faces and radiation symbols for different hours]