Optical Biopsy with Patent Blue V for Head and Neck Cancer Imaging

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Workshop on Intra-Operative Assessment of Tumor-Resection Margins
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Probe based Confocal Laser Endomicroscopy

- Fibered confocal laser technology – Cellvizio® MaunaKea Technologies
- 60µm depth
- 660nm
- NIR Contrast agent – Patent Blue V
MEC-ORL ex vivo study: Patent Blue V images

Confocal lab | pCLE | HES
---|---|---
Patent Blue V

With gastroflex UHD probe

Squamous epithelium
Partial squamous metaplasia
Poorly differentiated squamous cell carcinoma
pCLE & head and neck cancer: Potential applications

Development of new imaging strategies for:

• Diagnosis
  - Precancerous and cancerous lesions
  - Biopsy guide

• Therapeutic
  - Improve the definition of the resection margins
  - Response to targeted therapy

• Follow up

Development of a clinical study: MEC-ORL Study  “MicroEndoscopie Confocale”

Multidisciplinary team: Pathologists, Imaging engineers & Head and neck surgeons
MEC-ORL study: Objectives

- **Main objective**
  - to validate the clinical value of pCLE in the management of patients with head and neck cancer by a better definition of the resection margins.
  - pCLE - "a virtual extemporaneous exam" - will be compared to the gold standard (conventional histology with H&E staining).

- **Secondary objectives**
  - Assessing the contribution of pCLE to improve the management of head and neck cancer by a better definition of the resection margins.
  - Toxicities and risks associated with pCLE and contrast agent.
MEC-ORL study: Inclusion & exclusion criteria

• Inclusion
  › Upper aero-digestive tract lesion
  › Small lesions (T1 ou T2)
  › Precancerous or cancerous

• Exclusion
  › Allergy to Patent blue V

• Open to inclusion since February 2013
  • n = 15/40
  › Resection (6 Larynx laser endoscopic resection, 3 Oral cavity)
  › Endoscopy (3 Larynx, 3 Oral cavity)

• Bicentric French study
  › Gustave Roussy Villejuif
  › CHU Toulouse
MEC-ORL study: Methodology

**Endoscopic pCLE procedure**

- **Patent blue V**

**Correlation study**

- Blind review of the pCLE images by 2 pathologists
- Conventional H&E histology

- pCLE images
MEC-ORL study: Endpoint

- **Diagnostic concordance** between the **intraoperative pCLE images** (read by a pathologist) and the **conventional histological analysis on H&E**

- **Primary endpoint**
  - **Major concordance:** two classifications leading to the same therapeutic action (treatment or no treatment)

- **4 categories:**
  - **Cancerous lesions:** invasive SCC, micro-invasive squamous cell carcinoma, other non-SCC cancerous lesion
  - **Pre-cancerous lesions:** leukoplakia, low-grade and high-grade dysplasia, *in situ* carcinoma
  - **Non-cancerous lesions:** normal tissue, inflammatory tissue, necrosis, fibrosis, benign tumour…
  - **Non classifiable**
MEC-ORL study: Technical challenge

- Accessibility of to the lesion
  - Head and neck examination conditions
MEC-ORL study: Technical challenge

- Lack of pointing precision
  - High number of unclassifiable images on the 5 first patients
  - Flexibility of the probe
  - Freely handled
  - Precise positioning of the probe
  
  → Stabilization of the probe through the use of a cystoscope combined with an Albarran lever (Dr C. Betz – Germany)
MEC-ORL study: Representative images – Normal tissues

- Normal squamous epithelium
- Normal respiratory epithelium
- Dorsal part of the tongue
  = Trap for the pathologists
MEC-ORL study: Representative images - Cancer

Squamous cell carcinoma

Major challenge: infiltrating or not??
MEC-ORL study: Analysis challenge

- **Good point**
  - Very good assessment of the normal tissue

- **Analysis challenge**
  - No distinction between carcinoma in situ or infiltrating carcinoma

- **Tumor margin assessment**
  - one option: if carcinoma close to the macroscopic tumor → resection?
MEC-ORL study: Conclusion

- Clinical diagnosis study

- Technical challenge
  - improvement through the stabilization and stiffening of the probe
  - probe not dedicated to head & neck

- Analysis challenge
  - Infiltrating or not

- Tumor margin assessment
  - Not yet useful in daily practice
  - Combination with robotic surgery?
  - Combination with other imaging techniques?
Ongoing preclinical innovative approach

**Full field OCT (FFOCT)** - Deeper analysis without contrast agent

- **Histology based diagnosis**
  - 5 days needed

- **FFOCT image**
  - Light-CT scanner by LLtech
  - Dozen minutes

- **Optical biopsy on Head&Neck tissue using Full-Field OCT: a pilot study.**

- **Stromal reaction**
- **Striated muscles**
- **Carcinoma nest**
Thanks to

The patients who give their consent

At Gustave Roussy:

Imaging and Cytometry Platform

The technicians of the Biopathology Department

The nurse in the operating room

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