Novel Multimodal Imaging in Oral Medicine

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The Mouth

- A window into the body
- Easy access
- Can study pathology of both hard and soft tissue:
  - Oral cancer
  - Fluid-filled lesions
  - De-mineralisation

Representative Biopsy Sampling

• Despite readily accessible tissue, biopsy sites are chosen by visual inspection
• Histological diagnosis
• Is this representative?
• What can we do to help?

Enhanced Visualisation of Potentially Dysplastic Tissue

Toluidine blue staining  Autofluorescence  Chemiluminescence  Direct Oral Microscopy
Limitations of Visualisation Adjuncts

- Highly subjective and qualitative
- Indirect evaluation of diagnostic histopathological features
- Low specificity culminating in biopsy sampling errors

Motivations

- To establish a quantitative parameter which reflects the underlying diagnostic features evident in OED and fluid-filled lesions histology
- To present data in a clinically accessible format
What can 2D OCT ‘see’?

- Answer: Lots of speckle!
- Where is the morphology?
What can 3D OCT ‘see’?

- Surface topology
- Useful for recording appearance, i.e.
  - Tumour size
  - Papilloma
- 3D representation does not readily display internal morphology
Oral Epithelial Dysplasia (OED)

- Lesions can be benign, pre-malignant or malignant
- Ambiguous clinical presentation
- Diagnosis via invasive biopsy of representative site
- Biopsy site visually selected

Oral epithelial dysplasia is a pre-malignant condition that presents this diagnostic challenge

**White lesion**  **Red lesion**
OED Histology

OED severity is graded based on cellular and architectural changes within the epithelial layer.

Examples include:
- Increase in the nuclear to cytoplasmic ratio
- Prominent and super-basal mitosis
- Abnormal variation in nucleoli and nuclear size and shape
- Increased cellular density

**Images:**
- Mild dysplasia
- Moderate dysplasia
- Severe dysplasia
OCT of Oral Dysplasia

Nuclear **staining** intensity (Histopathology)

Nuclear **scattering** intensity (OCT)

Normal

Severe Dysplasia

Intensity (a.u.)

Depth
Quantitative Analysis

Histology

ROI Selection

Staining Gradient distribution

Quantitative Analysis

The normal/mild samples (a) displayed a high degree of colour homogeneity compared with the moderate/severe dysplasia samples (b)

Sensitivity and Specificity

The distribution of A-Scan gradients alone yielded a sensitivity and specificity of 74%.

Mode gradient of each B-Scan achieved 90% sensitivity and specificity.
Oral Fluid-Filled Lesions

- Clinical diagnosis can be challenging
  - A plethora of aetiological factors i.e. infection, inflammation, trauma
  - Multiple independent lesions can present similar clinical findings
- Diagnosis via invasive biopsy and histological examination
- Difficulty in selecting biopsy site crucial for establishing diagnosis
- Regular follow-up to monitor treatment is also fraught with difficulty
OCT of Oral Fluid-Filled Lesions
OCT of Oral Fluid-Filled Lesions

OCT A-Scan

Cumulative Intensity

Intensity (dB)

Attenuation Depth (AD)

Intensity Drop (ID)

$SID = \frac{ID}{AD}$

Percent of Total (%)

Depth (mm)

5% Backscatter

90% Backscatter

www.smd.qmul.ac.uk
Scaled Intensity Drop (SID) Microscopy

Sensitivity and Specificity

![Histogram and S-D curve](image)

- Frequency vs. Scaled Intensity Drop (dB/mm)
- Percent vs. SID Threshold (dB/mm)
Measuring Hard Tissue (Teeth)

Demineralised Enamel (Early caries)

Remineralisation
Custom Made Device

- Hand held
- Real-time acquisition and display (fast)
- 3D Acquisition
- Large area scanning >1cm²

Solution

- 100kHz line rate – 200 2D images per second
- Volume rates (500x500x500 pixels in 5 seconds)
- GPGPU real-time OCT data processing
- Current scan size limited to ~1 cm²
Summary

• Directly correlated OCT scattering profile with underlying histological features of OEDs and fluid filled lesions

• We have used this to form quantitative ‘SAM’ and ‘SID’ images of OED and fluid-filled lesions respectively

• We have applied the ‘SAM’ principle to investigate early caries and re-mineralisation of human enamel

• Developed and patented a custom made in vivo imaging device for quantitative clinical evaluation of oral diseases

OK Adegun et al, WO2012059723 Scanning Methods and Apparatus
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