Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER362
Topic:	Autofluorescence imaging of oral mucosal abnormalities
Summary of findings:	This report investigates autofluorescence imaging, as an adjunct to conventional visual examination, to diagnose dysplastic and malignant oral lesions. HTW identified a number of meta-analyses, with large numbers of participants, which reported that adjuvant autofluorescence imaging may provide higher sensitivity but lower specificity, compared to conventional visual examination alone, in the diagnosis of dysplastic and malignant oral lesions. Secondary evidence suggests that adjuvant autofluorescence may provide some benefit in identifying malignant or premalignant lesions, but leads to an increase in biopsies due to low specificity. Whilst a large body of secondary evidence was identified, it is unclear how many of the included studies were randomised controlled trials and most studies used one type of device (VELscope). We did not identify any evidence reporting outcomes other than diagnostic accuracy. Further investigation may be warranted to identify the certainty of the evidence and to assess whether use of autofluorescence leads to improved clinical outcomes. We did not identify any economic evidence.

Introduction and aims

Oral cancer is most commonly characterised by oral mucosal abnormalities, such as mouth ulcers that do not heal and unexplained lumps in the mouth or upper neck. The current procedure for identifying whether this tissue is malignant or premalignant consists of visual inspection, followed by biopsy for any areas of concern. Benign lesions may present very similarly to early malignant or premalignant lesions, which makes it difficult to distinguish between them.

Autofluorescence imaging works on the principle that certain biofluorophores present within the tissue become fluorescent on excitation with a suitable wavelength light source. Abnormal tissues tend to appear darker since they lose fluorescence, and it is suggested that identification of malignant or premalignant tissue could be improved with use of this technology, either by helping to identify the optimal biopsy site, or allowing detection before visual detection is possible.

OralID is one such autofluorescence imaging device, submitted by the topic proposer, but other devices exist, including VELscope and Identafi 3000. OralID is a battery-operated, hand-held oral examination light used as an adjunctive device for oral mucosal screening. The device emits a visible blue light (435 to 460 nanometres [nm]) that is shined directly into the oral cavity. Special OralID eyewear allows the clinician to view the tissue fluorescence during the oral exam.

Health Technology Wales researchers searched for evidence on adjunctive autofluorescence imaging of oral mucosal abnormalities to identify malignancy or premalignancy, including, but not limited to, OralID.

Evidence overview

HTW researchers identified a large number of meta-analyses assessing the diagnostic accuracy of autofluorescence imaging in combination with visual examination. The majority of these studies involved the VELscope device; we therefore also searched for primary evidence for OralID and Identafi 3000. This search revealed only one randomised controlled trial for OralID.

We did not identify any evidence reporting outcomes other than diagnostic accuracy (e.g. time to diagnosis or adverse events).

Guidance

A horizon scanning report by Adelaide Health Technology Assessment did not warrant further assessment of VELscope for oral cancer screening due to the quantity and certainty of the evidence they identified (Ellery et al. 2010).

Secondary evidence

A network meta-analysis by Kim et al (2021) compared the diagnostic accuracy of various tools (autofluorescence, chemiluminescence, cytology, narrow band imaging, and toluidine blue) with visual examination or other tools. The results of the network meta-analysis showed that autofluorescence, chemiluminescence, and narrow band imaging had higher sensitivity compared with visual examination. However, autofluorescence and chemiluminescence had lower specificity compared with visual examination. There were no significant differences in positive predictive value and accuracy among the six interventions. Overall, autofluorescence had the lowest ranked probability for accuracy considering both sensitivity and specificity.

However, a meta-analysis by Buenahora et al (2021) found that autofluorescence devices displayed superior accuracy levels in the identification of premalignant lesions and early neoplastic changes

compared to clinical examination and a chemiluminescent test. In the autofluorescence test (n = 5,562 samples), sensitivity and specificity were 86% and 72%, respectively, and area-under-the-curve was 0.86 (95% confidence interval [CI]: 0.83 to 0.89).

Another meta-analysis by Dos Santos et al. (2022) evaluated autofluorescence using VELscope for early detection of potentially malignant oral disorders. The combined sensitivity was 74% (95% CI: 60 to 76%, p = 0.0001) and the specificity was 57% (95% CI: 52 to 60%, p < 0.0001). Similarly, a meta-analysis by Moffa et al (2021) included 2,076 oral cavity lesions diagnosed with autofluorescence-based systems and conventional oral examination. They reported a pooled sensitivity and specificity of 81.3% (95% CI: 74.3% to 87.5%) and 52.1% (95% CI: 36.9% to 67.1%), respectively

A meta-analysis by Chaitanya et al (2019) included randomised controlled trials of 1,176 people with early dysplastic changes of the oral cavity, with the majority of studies reporting a sensitivity greater than 70%. Chaitanya et al (2019) concluded that autofluorescence was best suited for clinicians with sufficient experience and training; they found that the diagnostic performance of the inexpert examiner was not significantly improved when using VELscope compared to conventional observation alone, obtaining a sensitivity of 0.40 (95% CI: 0.406 to 0.773) and a specificity of 0.80 (95% CI: 0.614 to 0.923) with VELscope, compared to a sensitivity of 0.53 (95% CI: 0.343 to 0.717) and specificity of 0.83 (95% CI: 0.653 to 0.944) in the inexpert diagnosis without VELscope.

Primary evidence

Saini et al. (2019) compared the diagnostic accuracy of OralID with conventional oral examination to conventional oral examination alone in 98 potentially high-risk oral cancer patients. After the examinations, a surgical biopsy sample was taken from both groups to confirm the diagnosis. The true positive potential malignant lesions observed in the group only assessed with conventional oral examination compared with biopsy reporting was 89.47%, whilst it was 95.24% in the group examined with oralID and conventional oral examination. The sensitivity reported in the group examined with conventional oral examination alone was 89.47%, and 97.56% in the group examined with OralID plus conventional oral examination.

Areas of uncertainty

Whilst a large body of secondary evidence was identified, it is unclear how many of the included studies are randomised controlled trials and so further investigation may be warranted to assess the certainty of the evidence. In particular, randomised controlled trials with longer follow-up times could help determine whether use of autofluorescence improves clinical outcomes. We did not identify any evidence reporting outcomes other than diagnostic accuracy (e.g. time to diagnosis or adverse events). Very few studies in the secondary evidence were conducted in the UK and generalisability of the findings to NHS Wales is uncertain. The majority of the evidence came from studies using the VELscope device, and it is unclear how this device differs from other autofluorescence imaging devices. One ongoing observational study investigating OralID was identified as being in progress, with an estimated completion date of November 2021 (NCT03555721, not yet published). No relevant economic evidence was identified.

Literature search results

Health technology assessments and guidance

NICE
No evidence found

Healthcare Improvement Scotland
No evidence found

Hand search published SIGN Guidelines
No evidence found

Health Information and Quality Authority
No evidence found

EUnetHTA
No evidence found

International HTA Database

Ellery B, Mundy L, Hiller JE (2010). Adelaide Health Technology Assessment. Velscope for oral cancer screening: https://database.inahta.org/article/10974

International Guidelines Library
No evidence found

FDA
OralID (2014): https://www.accessdata.fda.gov/CDRH510K/K123169.pdf
Identafi 3000 (2009): https://www.accessdata.fda.gov/cdrh_docs/pdf9/K090135.pdf
VELscope (2010): https://www.accessdata.fda.gov/cdrh_docs/pdf10/K102083.pdf

Evidence reviews and economic evaluations

https://ksrevidence.com/
Buenahora, M.R., Peraza-L, A., Díaz-Báez, D., Bustillo, J., Santacruz, I., Trujillo, T.G., Lafaurie, G.I. and Chambrone, L., 2021. Diagnostic accuracy of clinical visualization and light-based tests in precancerous and cancerous lesions of the oral cavity and oropharynx: a systematic review and meta-analysis. Clinical Oral Investigations, 25(6), pp.4145-4159. https://doi.org/10.1007/s00784-020-03746-y

Chaitanya, N.C., Chavva, S., Surekha, E., Priyanka, V., Akhila, M., Ponnuru, H.K. and Reddy, C.K., 2019. A meta-analysis on efficacy of auto fluorescence in detecting the early dysplastic changes of oral cavity. South Asian Journal of Cancer, 8(04), pp.233-236. DOI: 10.4103/sajc.sajc_336_18

Dos Santos, L.C.F., Fernandes, J.R., Lima, I.F.P., da Silva Bittencourt, L., Martins, M.D. and Lamers, M.L., 2022. Applicability of autofluorescence and fluorescent probes in early detection of oral potentially malignant disorders: a systematic review and meta-data analysis. Photodiagnosis and Photodynamic Therapy, p.102764: https://doi.org/10.1016/j.pdpdt.2022.102764

Kim, S.W. and Hwang, S.H., 2021. Efficacy of non-invasive diagnostic methods in the diagnosis and screening of oral cancer and precancer. Brazilian journal of otorhinolaryngology. https://doi.org/10.1016/j.bjorl.2020.12.019

Moffa, A., Giorgi, L., Costantino, A., De Benedetto, L., Cassano, M., Spriano, G., Mercante, G., De Virgilio, A. and Casale, M., 2021. Accuracy of autofluorescence and chemiluminescence in the diagnosis of oral Dysplasia and Carcinoma: A systematic review and Meta-analysis. Oral Oncology, 121, p.105482: https://doi.org/10.1016/j.oraloncology.2021.105482

Ongoing research
https://scanmedicine.com/clinicaltrials Observational study: in 50 people presenting with a potentially malignant oral lesion for whom a biopsy is deemed necessary: https://clinicaltrials.gov/ct2/show/record/NCT03555721?view=record
OralID website
Saini, R., Cantore, S., Saini, S.R., Mastrangelo, F., Ballini, A. and Santacroce, L., 2019. Efficacy of fluorescence technology vs conventional oral examination for the early detection of oral pre-malignant lesions. A clinical comparative study. Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders), 19(6), pp.852-858: https://doi.org/10.2174/1871530319666190119103255

Date of search:	May 2022
Concepts used:	Autofluorescence imaging (AFI)/spectroscopy, fluorescence exam, oral examination, oral mucosal screening, oral autofluorescence, OralID, Identafi 3000 Ultra, VELscope, visualisation-enhancement adjunct