APPLICATION OF NANOTECHNOLOGY IN DIAGNOSIS OF ORAL CANCER - A SYSTEMATIC REVIEW

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INTRODUCTION

Oral cancer is a debilitating disease associated with metastasis, and a high recurrence and mortality rate.[1]

It is the sixth most common cancer, with the majority being oral squamous cell carcinoma.[2]

Nanoparticles usually target cells by receptor-mediated binding or endocytosis, and a nanoparticle surface modified with a ligand can efficiently bind with target cells. Surface functionalization of gold nanoparticles by conjugation with a specific agent such as an aptamer, peptide, antibody, and protein has been proposed for diagnosis and thermo-phototherapy of cancer cells.[3]

MATERIALS AND METHODS

The PubMed/ MEDLINE, EMBASE and CENTRAL databases were searched for works published from January 2005 to June 2020 using keywords "oral cancer diagnosis and nanotechnology"

Original retrospective and prospective clinical studies were included. Only articles published in the English language were selected. Bibliographies from previous systematic reviews on the topic were also analysed.

Articles for which full text could not be recovered, commentaries, editorials, and debates were excluded.

A total of 10 articles were included in this review

RESULTS AND DISCUSSION

AUTHOR	WORK
Li et al., 2006 [4]	Demonstrated water-soluble quantum dots conjugated with biotin and PEG in human tongue cancer cells for immunofluorescent labeling of cancer cells.
Photostability comparison between quantum dots and conventional FITC dye showed that the quantum dots are 1.5 times as bright at the beginning and increased to almost 50 times after 30min, which will be particularly valuable for quantitative fluorescent molecular detection and cell imaging of cancer cells.	
Kah *et al.*,2007[5]	Demonstrated the potential of antibody conjugated gold NPs to target and illuminate cancer cells under a reflectance-based optical imaging system.
Reported that gold nanoparticles could elicit an optical contrast to discriminate between cancerous and normal cells and their conjugation with antibodies allowed them to map the expression of relevant biomarkers for molecular imaging under confocal reflectance microscopy.	
Sharma *et al.*, 2010 [6]	Demonstrated quantitative single receptor level detection of the specific markers and CD63 receptors on individual exosomes from human saliva via targeted antibody tip coated force spectroscopy and antibody-labeled (antiCD63 IgG) gold nano beads.
Reported the distinct substructure of single isolated sub-100 nm human saliva exosomes in the form of trilobed structures and demonstrate their reversible elastic nanomechanical properties, which are useful as novel biomarkers for detection of cancer.	
Weigium *et al.*, 2010 [7]	Nano-bio-chip labeled with anti-EGFR monoclonal antibodies provide rapid detection and quantitation of EGFR biomarker in exfoliative cytology specimens.
Four key parameters were significantly elevated in both dysplastic and malignant lesions relative to healthy oral epithelium, including the nuclear area and diameter ($P < 0.0001$), the nuclear-to-cytoplasmic ratio ($P < 0.0001$), and EGFR biomarker expression ($P < 0.03$).63% (20 of 32) of SCC tumours and 67% (4 of 6) of precancerous dysplastic lesions overexpress the EGFR biomarker, whereas none (0 of 3) of the benign specimens exhibit biomarker overexpression.	
Wang et al., 2013 [3]	GNRs conjugated with Rose Bengal demonstrated rapid and quantitative detection of oral cancer cells based on near infrared absorption in Human OSCC cell line CAL27 and Tca8113.
This assay is label free and therefore is less labour intensive compared to the conventional diagnostic techniques like ELISA, micro-satellite analysis, and high-performance liquid chromatography (HPLC).	
Luke et al., 2014 [8]	In photoacoustic imaging, plasmonic nanosensors offer a rapid and effective tool to identify micrometastases in a metastatic murine model of OSCC.
Lymph node metastases as small as 50 µm were detected at centimeter-depth range with 100% sensitivity and 87.5% specificity. The findings offer a rapid and effective tool to identify micrometastases as an alternate to sentinal node biopsy analysis.	
Saxena *et al.*, 2015 [9]	Briefly described the architecture of the nanorobots which will augment the surgeon's motor performance, diagnostic capability, and sensations with haptics and augmented reality.
Research into nanorobots is still in its preliminary stages; the promise of such technology is endless.	
Jiang et al., 2015 [10]	The expression spectrum of salivary peptides in 40 T1 stage OSCC patients (and healthy controls) using MALDI-TOF-MS combined with nano magnetic beads was demonstrated.
Fifty proteins showed significantly different expression levels in the OSCC samples ($P<0.05$). The novel diagnostic proteomic suggested mass peaks of 1285.6 and 1432.2 Da which were both identified as histatin-3 in saliva as correlated with OSCC progression.	
Ankri *et al.*, 2016 [11]	The airSEM pictures presented a gradient of GNRs from the tumour to normal epithelium spread in an area of 1 mm, suggesting tumour margins of 1 mm. There was a clear difference between the DR profiles of the healthy epithelium and the tumor
The presented method supplies an objective tool for the tumour margins determination, based on anti-EGFR-GNRs actual visualisation with a detection resolution of 1 mm.or margins identification.	
Asifkhan et al. 2017 [12]	Combined the folate preconjugated chitosan and magnetic poly (lactide-*co*glycolide) (PLGA) nanoparticles to create an MRI contrast agent . Shortens the overall T2 relaxation time and provides better in vitro MR imaging
The relaxivity value of fcMagP nanoparticles was found to be 232.7 mM1 s1, which is much better than commercial contrast agent, ferumoxytol (85 mM1 s1)	

PEG: Poly Ethylene Glycol, FITC: Fluorescin isothiocyanate, NP: Nano particle, EGFR: Epidermal growth factor receptor, SCC: Squamous cell carcinoma, GNRs: Gold nanorods, OSCC: Oral squamous cell carcinoma , MALDI- TOF-MS : Matrix-assisted laser-desorption ionization–time-of-flight–mass spectrometry AirSEM: Air scanning electron microscopy, DR: Diffusion reflection, PLGA: Poly lactide-co glycolide, MRI:Magnetic Resonance Imaging, MR: Magnetic Resonance

CONCLUSIONS

Nano-based diagnostic methods using quantum dots, gold nanoparticles, nano biochips, plasmonic nanosensors, and nanorobots seem to be promising tools to provide rapid and real-time diagnosis for oral cancer. However, the methodologies and clinical results vary within and between each of the studies included in this review. Therefore, it is difficult to conclude and support the superiority of one diagnostic method over another. Further well-designed medium to long term studies are required to define the benefit of nanotechnology in the early diagnosis of oral cancer with good clinical results.

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