

**Thematic Area**

Prevention and Epidemiology (Scaling up research)

**Title of the Proposed research project**

Validation of OralScan device in detection of Oral Premalignant Lesions

**Rationale**

Oral cancer is major public health problem in the Indian subcontinent, where it ranks among the top three types of cancer. The bottom of pyramid population is most affected due to exposure to well known risk factors such as tobacco, smoking, alcohol, gutka and pan. Studies have shown that use of smoking and smokeless forms of tobacco are significantly higher in the rural and tribal areas, among uneducated poor people, and the socially disadvantaged castes.

Typically, precancerous stage is the most common clinical manifestation prior to full blown malignant oral cancer. So, detection during precancerous stage assumes great significance as early detection and prompt treatment can save patients from mortality and reverse the transition to cancer with concurrent removal of risk factors. These precancerous lesions are credible indicators of an impending progression into oral cancer and they provide us with a window of opportunity to undertake screening for oral cancer.

Since these lesions are asymptomatic in precancerous stage, patient does not seek care and often remains undetected until higher stages of malignancies are reached. Sensitivity of traditional methods of visual inspection with light has poor diagnostic value. Thus, there is a need to develop sensitive techniques to screen and detect oral precancers

Sascan has developed OralScan - a novel hand-held intraoral imaging camera to non-invasively screen and detect oral precancers. The procedure takes less than 5 minutes for cancer screening and provides results of screening in real-time at the point of care with the help of a cloud-based machine learning algorithm. OralScan is developed with BIG-BIRAC funding and has been tested and validated through multicentric clinical studies.

**Describe the current knowledge available on the subject, critical gaps in knowledge and the national relevance of the research question which this project aims to address. Also mention the preliminary work done by the applicant, if any.**

It is quite clear that the incidence of oral cavity cancer can be reduced by timely screening, treatment and follow-up. More specifically, to reduce morbidity and mortality associated with oral cancer, the awareness creation and habit cessation programs must continue and enhance the preventive health-seeking behaviour among high-risk individuals. Screening of a higher proportion of individuals in the target group, providing advice and treatment to all individuals with an oral potentially malignant diseases and collection of service delivery statistics will facilitate monitoring and evaluation of ongoing program activities and outcomes.

A reduction in the oral cancer burden in the country would lead to a lowering of the expenses incurred by the existing public healthcare system and shift the focus to a prevention-oriented approach than treatments based on surgery, that often leads to functional deficits and radiation treatments.

The OralScan device was indigenously developed by Subhash Narayanan of Sascan, who has been working on cancer diagnostics using optical techniques for more than a decade. He founded Sascan in 2015 and have been involved in prototyping and developing a hand-held multispectral imaging intra-oral camera for the first time in the world for oral cancer detection and biopsy guidance. The device uses multiple LEDs to illuminate the tissue and captures fluorescence images from biochemical constituents of tissue, such as FAD and PpIX, along with images of oxygenated haemoglobin absorption in the diffusely reflected light to screen and detect squamous cell carcinomas of the oral cavity. Proprietary software is developed to operate the device and process the captured images in real time. Cloud based machine learning algorithm is used to assess the cancer grade at the point of care during the screening process. The indigenous technology developed has received an Indian Patent in 2018 and the US patent is pending.

The PoC and Phase 1 clinical studies are completed, and Phase 2 clinical studies are ongoing at 6 centres to validate the device. Till now, OralScan has touched the lives of around 500 people and provided biopsy guidance to more than 60 patients with potentially malignant diseases in their oral cavity. The machine learning algorithm that correlates the results of histopathology with the oxygenated haemoglobin absorption ratio R610/R545 has

demonstrated a sensitivity of 78% and specificity of 90%, Positive Predictive Value: 87% Negative Predictive Value:81% for discrimination between normal and precancerous tissue sites.

**Novelty/Innovation (up to 100 words): Describe how the proposal challenges and seeks to shift the current research/knowledge/clinical practice paradigms by utilizing novel theoretical concepts, methodologies, instrumentation or interventions.**

Innocuous precancerous lesions are traditionally assessed by visual examination with normal white light. Biopsy followed by histopathology is the gold standard for cancer diagnosis. However, it all depends on the obtaining the right sample which is subjective technique.

Since the OralScan device is portable, non-invasive and can be operated by trained health workers, they also stand to benefit economically from screening.

**Project description (up to 600 words): Describe the study setting, study design, sampling strategy, sample size, research methodology and outcomes measures. Also mention expected timelines, total budget, name and designation of co- investigators and intra and inter institutional collaborations, if any.**

#### ***Study setting***

This research project will be conducted in the tribal areas of Wayanad district in Kerala. This population was chosen because of the high prevalence of oral pre-malignant lesions.

#### ***Study design***

This community-based trial is designed to assess the diagnostic accuracy of OralScan device.

#### ***Sampling strategy***

Cluster sampling technique will be adopted for the study. Each tribal hamlet with a minimum population of 100 within 40 km radius around Kalpetta town of Wayanad district will be considered as a cluster. The clusters will be selected at random. Every person in the cluster present at the time of data collection will be approached for participation in the study.

### ***Sample size***

The results of Phase 1 and 2 trials have demonstrated a sensitivity of 78% for OralScan. The sensitivity of traditional visual examination is about 60%. Sample size was calculated using test for Diagnostic accuracy of screening test (nMaster 2.0). The minimum sample size was estimated to be 102. It will be increased to 150.

The prevalence of pre-malignant lesions among Paniya tribes was 0.8%. To achieve a sample size of 150 participants with pre-cancerous lesions, a minimum of 1500 participants need to be screened.

### ***Study methodology***

#### *Inclusion criteria:*

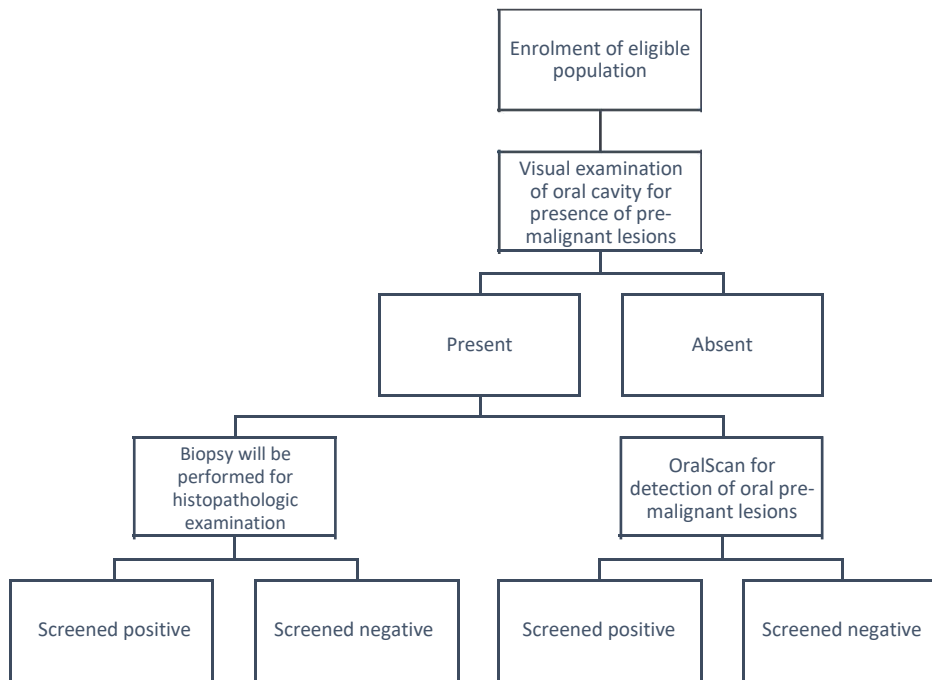
All study participants showing signs of early dysplasia (asymptomatic, red or white lesions, non-healing ulcer for more than 2 weeks) would be considered as premalignant lesions by visual examination (n = 150). The same cases would be subjected to detection using OralScan device and based on its colour scheme (output) would be classified as screening positive or negative.

Study participants classified as having pre-malignant lesions based on visual examination would then undergo a biopsy for histopathological examination for dysplastic features and will categorized as screened positive and screened negative.

Diagnostic accuracy analysis (sensitivity, specificity, positive predictive value, negative predictive value, yield and ROC curve) will be performed between the diagnostic outcome of histopathology and OralScan.

#### *Exclusion criteria:*

Study participants showing obvious signs and symptoms of malignant lesions will be excluded.



- *Risk factor analysis, supportive care and follow up will be facilitated for patients testing positive for premalignant lesions*

**Outcome measures:**

1. Clinical Effectiveness related indicators
  - a. No of people screened
  - b. Early stage cancer detected (No of lives saved)
  - c. Improvement in screening accuracy
  - d. Sensitivity and Specificity of the diagnostics value
  - e. Predictive value of the diagnostic instrument
  - f. Lead time Gain
  - g. Prevalence and Incidence of various types of precancerous lesion of oral cavity
  - h. Quality Adjusted Life Years (QALY)
2. Economic Indicators
  - a. Cost benefit Analysis
  - b. Cost effectiveness analysis
  - c. Cost utility analysis
  - d. Cost consequence analysis

- e. Budget Impact Analysis
  - f. Net health benefit
3. Socio-cultural indicators
- a. Ethics of screening earlier
  - b. Acceptance of the Screening technique by patients
  - c. Health workers ease of use of instruments

***Timeline***

Activity	Length of activity in months	Target
Manufacture and Supply of OralScan for field studies	6	To initiate oral cancer screening programs in identified field sites
Ethics Approval for Study from Amrita Institute of Medical Sciences, Kochi	6	To initiate oral cancer screening programs in identified field sites
Development of Sampling frame, and coordination with tribal population	5	To initiate oral cancer screening programs in identified field sites
Follow up of the project sites (support to the cases that reported positive during screening)	12	Determination of diagnostic accuracy of screening
Final Analysis of data and Report write up	6	Project completion report

***Total Budget***

53 lakhs

***Co-investigators***

Dr Subhash Narayanan is a PhD in Laser Physics. He has been working in the area of cancer detection using non-invasive optical techniques for the past 10 years and has published more than 40 papers in peer-reviewed international journals, mostly relating to clinical

studies for detection of early stages oral and cervical cancers using devices developed by his group. He has filed 3 patent applications on oral cancer detection. As part of the clinical studies carried on various types of oral diseases and cervical cancer screening, he and his team had the opportunity to work with BOP communities.

Dr. R Venkitachalam is Assistant Professor at Amrita School of Dentistry and a Dental Public Health Expert experienced in managing clinical trials and health system analysis.

Dr. Mahija Janardhanan is a Professor at Amrita School of Dentistry. She is an Oral Pathologist. Her areas of interest include oral cancer diagnosis.

#### ***Inter-institutional collaborations***

- Sascan Meditech Pvt Ltd –Supply of OralScan device  
A-503, Sowparnika Purple Rose, off Chintamani Road, Yelachanayakanpura, Hoskote, Bangalore –562114
- Amrita Kripa Charitable Hospital Kalpetta, Wayanad –base camp for study setting
- Reseapro Scientific Services Pvt Ltd., Bhubaneswar - Clinical study coordination

**6. Strength of PI: Describe academic qualifications, employment details, previous experience of handling research projects (past and ongoing) and the scientific contributions made from these projects. Enumerate 10 relevant publications (in Vancouver style).**

Dr Chandrasekhar Janakiram is a PhD in Epidemiology and Public Health, with 57 publications and many awards. He was coordinator for National Oral Survey of India and has been working in Public Health surveillance, oral diseases epidemiology and has considerable experience to conduct large scale screening and health technology assessment. The PI has also been the Program Coordinator for various welfare programs for the tribal communities viz. Amritasmitham free denture program for the past 10 years, Coordinated School Health Program among tribal school children and tobacco cessation activities. Presently the team under PI is also working on Oral Disease Vulnerability Index mapping of tribal hamlets in Wayanad which focuses on the use of technology like GPS enables applications and GIS softwares for data collection and representation.

The PI was also a consultant for primary oral health care project for government of Kerala and Karnataka. The PI also has experience as research fellow in Health Informatics from the prestigious National Institute of Dental and Craniofacial Research, National Institutes of Health, United States of America.

#### Publications

1. Chandrashekar Janakiram; Vinita Sanjeevan; Joe Joseph. Intergenerational Transfer of Tobacco Use Behaviour from Parent to Child: A Case Control Study. *Asia Pacific Journal of Cancer Prev* 2019; 20(10):3029-3035.
2. Janakiram C, Taha F. Ethics of dental health screening. *Indian J Med Ethics*. 2016 Sep;1(3):171–Valsan I, Joseph J, Janakiram C, Mohamed S. Oral Health Status and Treatment Needs of Paniya Tribes in Kerala. *J Clin Diagn Res JCDR*. 2016 Oct;10(10):ZC12–5.
3. Janakiram C, Joseph J, Vasudevan S, Taha F, Deepan Kumar Cv, Venkitachalam R, et al. Prevalence and Dependency of Tobacco Use in an Indigenous Population of Kerala, India. *J Oral Hyg Health* [Internet]. 2016 Feb 7 [cited 2017 Jan 6]; Available from: <http://www.esciencecentral.org/journals/prevalence-and-dependency-of-tobacco-use-in-an-indigenous-populationof-kerala-india-2332-0702-1000198.php?aid=69141>
4. Deepan Kumar CV, Mohamed S, Janakiram C, Joseph J. Validation of dental impact on daily living questionnaire among tribal population of India. *Contemp Clin Dent*. 2015 Sep;6(Suppl 1):S235–41.
5. Venkitachalam R, Chandrashekar Janakiram, Jos Joseph, Vinita Sanjeevan, Bobby Anthony, Vineetha K., HeljoPadamadan, Sravan Kumar Y. Community Health Diagnosis in a tribal hamlet in Kerala: A case study from India. *Community Health Diagnosis in a tribal hamlet in Kerala: A case study from India*. *Indian Journal of Public Health Research And Development*. (accepted for publication in 2019 issue).
6. Janakiram C, Antony B, Joseph J, Ramanarayanan V. Prevalence of Dental Caries in India among the WHO Index Age Groups: A Meta-Analysis. *J Clin Diagn Res* [Internet]. 2018 [cited 2019 Jan 4]; Available from: [http://jcdr.net/article\\_fulltext.asp?issn=0973-709x&year=2018&volume=12&issue=8&page=ZE08&issn=0973-709x&id=11956](http://jcdr.net/article_fulltext.asp?issn=0973-709x&year=2018&volume=12&issue=8&page=ZE08&issn=0973-709x&id=11956)



7. Janakiram C, Ramanarayanan V, Sanjeevan V, Varghese NJ. Comparison of Plaque Removal Efficacy of Tooth Powder and Too Randomized Controlled Clinical Trial. :7.
8. Janakiram C, Sanjeevan V, Br R, Joseph J, Stauf N, Benzian H. Political priority of oral health in India: analysis of the reasons for neglect. J Public Health Dent. 2018 Mar;78(2):144–53.
9. Janakiram C, Venkitachalam R, Joseph J. Understanding Oral Health Systems [Internet]. LAP LAMBERT Academic Publishing; 2016 [cited 2017 Jun 18]. Available from: <https://www.morebooks.de/store/gb/book/understanding-oral-health-systems/isbn/978-3-659-97735-0>
10. Janakiram C, Chalmers NI, Fontelo P, Huser V, Lopez Mitnik G, Iafolla TJ, et al. Sex and race or ethnicity disparities in opioid prescriptions for dental diagnoses among patients receiving Medicaid. J Am Dent Assoc 1939. 2018 Apr;149(4):246–55.

**7. Institutional support (up to 200 words): Mention the institutional support in terms of basic infrastructure, departments and laboratories with equipment required for the proposed research work.**

Amrita institute of Medical Sciences and Research Center functions under the aegis of Mata Amritanandamayi Math. It is a well-known name for its medical, educational, research, outreach and philanthropic activities. The hospital has an outreach centre named Amrita Kripa Charitable Hospital at Kainatty, Kalpetta, Wayanad catering mainly to the tribal population. This center will act as one of the base camps for the project.

The study is being planned by the Dept. of Public Health Dentistry, Amrita School of Dentistry. The department manages the dental clinic at the Amrita Kripa Hospital. The Amrita Kripa Hospital also regularly conducts health check-up camps in the tribal hamlets and has a good rapport with the community. The center also has dedicated field and health workers who can act as perceptors for the research team.

The research team from Dept. of Public Health Dentistry is also equipped with resources and manpower to collect and analyse data. The investigators have prior experience in undertaking projects in tribal areas. The team also has the technical

knowledge and expertise in conducting capacity building workshops for health workers as required for the project.