Fourier transform infrared for noninvasive optical diagnosis of oral, oropharyngeal, and laryngeal cancer

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The 5-year survival rate for advanced head and neck cancers is 50%. There is currently no noninvasive method or effective screening procedure available to diagnose head and neck cancer at the earliest stages when it is still highly curable. This study aims to show how Fourier transform infrared (FTIR) spectroscopy could be used as a sensitive, noninvasive, low cost technique to diagnose head and neck cancer at an earlier stage and, thus, increase the likelihood of survival. Sputum samples were collected from 16 cases with oral or oropharyngeal cancer, 8 cases with laryngeal cancer patients and 15 normal controls. Cell pellets were produced from each of these samples and used to generate FTIR spectra within the 'biochemical fingerprint' wavenumber region of 1800 to 950 cm^{-1}. Discrimination between cancer and normal sputum was achieved using infrared wavenumbers 1650 cm^{-1}, 1550 cm^{-1}, and 1042 cm^{-1} determined by robust feature selection. These 3 wavenumbers were used to develop potential models to discriminate both oropharyngeal and laryngeal cancer from normal control. In cancer cases, the absorbance levels for 1550 cm^{-1} were increased relative to controls, whereas 1042 cm^{-1} absorbance was decreased suggesting changes to protein and glycoprotein structure within sputa cells. This preliminary study shows potential for how FTIR could be developed into a simplistic diagnostic tool that could easily be implemented by a nonspecialist to diagnose and monitor head and neck cancer. The method could especially provide a means for detecting laryngeal cancer hidden from noninvasive observation. (Translational Research 2014;163:19–26)

Abbreviations: FTIR = fourier transform infrared; IR = infrared; PLS = partial least squares; RR = relative risk; SCC = squamous cell carcinoma; SD = standard deviation; SlimPLS = PLS method; UK = United Kingdom

Head and neck cancer represents the fifth most common cancer in men and eighth most common in women worldwide with about 600,000 new cases each year.[1] More than 90% of the cancers are of squamous origin, arising from any part of the upper respiratory tract. Tumors of the larynx have represented the largest proportion of cancers historically, but over the last few decades, the incidence

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AT A GLANCE COMMENTARY

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Background

The 5-year survival rate for advanced head and neck cancers is 50%. This study shows how optical spectroscopy, based on a small panel of infrared wavelengths, could be used as a sensitive, low cost technique to diagnose head and neck cancer at an earlier stage and thus increase the likelihood of survival.

Translational Significance

Fourier transform infrared (FTIR) spectroscopy could be developed into a simplistic diagnostic, tool that could easily be implemented by a nonspecialist to predict head and neck cancer especially for detecting laryngeal cancer hidden from noninvasive observation.

of oral/oropharyngeal disease has been rapidly increasing. In the United Kingdom (UK), oral/oropharyngeal disease now represents the highest burden of disease. Historically, smoking and alcohol have represented the main risk factors for head and neck cancer.[2] Most head and neck cancers associated with these risk factors arise in the 60+ group. There is a rising incidence in oral/oropharyngeal disease world-wide, which has been attributed to human papillomavirus infection. Recent studies, using postoperative radiotherapy and concomitant chemotherapy have been able to show a small improvement in survival,[3] but the 5-year survival of head and neck cancer patients, including oral and laryngeal, is still around 63%,[4] and is associated with high rates of morbidity and a severe impact on patients quality of life. Late presentation of lesions, lack of suitable markers for early detection, and failure of advanced lesions to respond to conventional treatments contribute to a poor outcome. The diagnosis of head and neck cancer is usually made after cytologic and/or histologic evaluation of biopsy specimens in symptomatic patients.

There is currently no method or effective screening procedure available to diagnose head and neck cancer at the earliest stages when it is still highly curable. A large-scale cluster-randomized controlled trial in India concluded that oral visual screening could reduce oral cancer mortality in high-risk cases.[5] An early detection for laryngeal cancer, where the tumor is hidden from noninvasive observation, is particularly desirable. In recent years, there has been increased interest in the development of optical diagnostic modalities for head and neck cancer.[6] Optical diagnostic devices use light of varying wavelength to detect differences between disease, and abnormal tissue that phenotypically might be similar. A recent review by Jerjes et al highlights a range of minimally invasive *in vitro* and *in vivo* optical diagnostic techniques that show promise to distinguish pathologic stages of head and neck disease including elastic scattering spectroscopy, differential pathlength spectroscopy, near-infrared spectroscopy, Raman spectroscopy, confocal reflectance microscopy, fluorescence imaging, microendoscopy, and optical coherence tomography.[7] One optical diagnostic method that has been evaluated in a number of studies for head and neck tissue is Raman spectroscopy.[8]

Raman spectroscopy relies on in-elastic light scattering. A Raman spectrum results from a shift in frequency in the incident excitation light above and below the wavelength of the incident photons. For biological tissue, the shift in frequency is due to the vibrational frequencies of the molecules, and structural change to these molecules could serve as a biomarker. The technique is able to distinguish between premalignant, malignant, inflammatory, and normal biopsy tissue.[9] Devpura et al have also used Raman spectroscopy to distinguish tissue, in situ, of normal and squamous cell carcinoma (SCC).[10] Harris et al have evaluated the sensitivity and specificity of Raman spectroscopy to detect head and neck cancer using peripheral blood samples with promising results.[11] Interestingly, 3 studies have demonstrated how Raman spectroscopy is able to differentiate between laryngeal and abnormal or normal biopsy tissue with high sensitivity and specificity.[12-14] Another study by Lau et al showed how Raman spectroscopy was able to classify tissue obtained from cancer and control cases in the nasopharynx.[15]

Any diagnostic method that is noninvasive has obvious benefits, and for head and neck cancer, a technology providing analysis of sputum would present an ideal diagnostic modality. Surface enhanced Raman spectroscopy has been previously used to determine biochemical changes in saliva of oral cancer cases. Whereas this technique was successful, it required the use of gold nanoparticles to enhance the Raman spectroscopy signal as otherwise the spectra are weak preventing adequate analysis.[16]

Another optical diagnostic technology with potential for head and neck cancer tissue discrimination is Fourier transform infrared (FTIR) spectroscopy. The principles of FTIR and how infrared (IR) light is absorbed by biomolecules are as follows. All atoms in a molecule are in continuous vibration relative to each other. If a certain frequency of IR radiation is directed onto a molecule