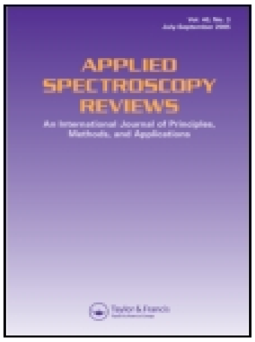

Applied Spectroscopy Reviews

ISSN: 0570-4928 (Print) 1520-569X (Online) Journal homepage: www.tandfonline.com/journals/laps20

Hyperspectral Imaging in the Medical Field: Present and Future

Mihaela Antonina Calin, Sorin Viorel Parasca, Dan Savastru & Dragos Manea

Applied Spectroscopy Reviews, 49:435–447, 2014

ISSN: 0570-4928 print / 1520-569X online
DOI: 10.1080/05704928.2013.838678

Hyperspectral Imaging in the Medical Field: Present and Future

MIHAELA ANTONINA CALIN,[1] SORIN VIOREL PARASCA,[2] DAN SAVASTRU,[1] AND DRAGOS MANEA[1]

[1]National Institute of Research and Development for Optoelectronics INOE 2000, Magurele, Ilfov, Romania
[2]Emergency Clinical Hospital for Plastic, Reconstructive Surgery, and Burns, Bucharest, Romania

Abstract: *Hyperspectral imaging is an optical method that provides a large amount of information about the investigated object. Its medical applications are reviewed in this article, including tumor delimitation and identification, assessing tissue perfusion and its pathological conditions (including some complications like diabetic foot ulceration), making accurate surgical decisions, evaluating the health of dental structures, etc. Many of the articles show very promising results that required brief comments by the authors. It is clear that choosing the appropriate hyperspectral imaging system for each medical field, together with the most reliable hyperspectral image processing methods, are the main goals of future studies, before hyperspectral imaging becomes a widely applicable evaluation method in medicine. The authors try to answer some questions on this topic and set up some directions for future research.*

Keywords: Hyperspectral imaging, cancer, diabetic foot ulceration, tissue oxygenation, intraoperative visualization

Introduction

Development of effective, noninvasive, and low-cost medical diagnostic techniques, especially imaging techniques, is a major challenge for researchers worldwide. Many medical imaging techniques based on the use of ionizing and nonionizing radiation or ultrasound for examination of organs and tissues have been developed to date. Imaging techniques such as X-ray computed tomography, positron emission tomography, nuclear imaging, magnetic resonance imaging, optical coherence tomography, fluorescence imaging, confocal microscopy, ultrasonography, etc., are now widely applied in medical clinics for accurate diagnosis of a wide range of conditions. Discovering new and specific techniques for more efficient diagnosis and monitoring of the treatment is currently a very active field of research. In recent years, researchers have focused their efforts particularly on developing noninvasive optical diagnostic techniques based on exploring the optical properties of tissues. Among the newer optical techniques, hyperspectral imaging (HSI) is very promising

Address correspondence to Mihaela Antonina Calin, National Institute of Research and Development for Optoelectronics INOE 2000, 409 Atomistilor Street, P.O. Box MG5, Magurele, Ilfov 077125, Romania. E-mail: antoninacalin@yahoo.com
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/laps.

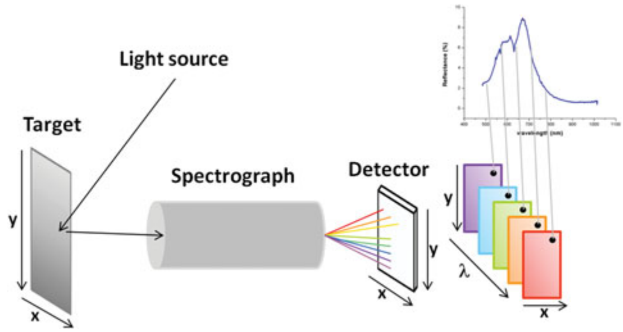

Figure 1. Schematic diagram of a hyperspectral imaging system.

for future medical applications. HSI combines the possibilities offered by spectroscopic techniques with the advantages of digital imaging. It consists of an acquisition of a series of images in many adjacent narrow spectral bands and reconstruction of reflectance spectrum for every pixel of the image (1). The set of images thus obtained (typically tens or hundreds of images) is called the *hypercube*. The image hypercube has three dimensions: two dimensions represent the spatial coordinate of a pixel and one dimension gives the wavelength of a particular spectral band. Thus, both spatial and spectral information about an object or scene under investigation can be obtained at the same time from analysis of the hypercube.

Hyperspectral images are produced by instruments called *hyperspectral imaging systems* or *imaging spectrometers*. These systems are built around three main components: a light source, a spectral separator (prism, grating, or optical bandpass filters, either tunable or fixed), and a detector (such as conventional 2D charge-coupled device [CCD]; Figure 1).

The light source is directed onto the surface of an object. After entering and passing through the object, the light is reflected, transmitted, and/or absorbed. The diffuse reflected light then passes through a spectral separator that spectrally discriminates the reflected light into a large number of spectral bands, typically tens or hundreds. Finally, the light reaches the detector, where it is collected as a two-dimensional image containing spectral data inherent in each pixel that is then transferred to a computer for further processing and analysis.

The hyperspectral imaging systems are used in a wide array of applications. Although originally developed for mining and geology, these systems are now used in fields such as agriculture (2), mineralogy (3), surveillance and target identification (4), astronomy (5), chemical imaging (6), and environmental studies (7). More recently, new potential uses of the hyperspectral imaging systems in the medical field have been suggested and evaluated, namely, their use as a noninvasive method for diagnosis and evaluation of therapeutic methods. This is because by measuring the reflection and absorption of light at different wavelengths, HSI has the ability to simultaneously provide information about different tissue constituents and their spatial distribution from the spectral signature of each pixel in the hyperspectral image. This ability of the HSI technique is currently used in the medical field for noninvasive detection of cancer, diabetic foot ulcers, and peripheral vascular disease and for assessment of tissue blood oxygenation levels during surgery.

This article aims to summarize the main clinical results and research reported in the literature concerning the effectiveness of HSI in diagnostis and evaluation of therapeutic methods. We limited our study to medical applications of hyperspectral reflectance imaging.

This study will try to answer the following five questions: (1) What type of diseases can be diagnosed with HSI? (2) Is HSI used in surgical procedures? (3) What kind of devices/parameters are used in medical applications? (4) What is the effectiveness of the HSI technique in the diagnosis and evaluation of therapeutic methods? (5) What are the future trends in the application of the HSI technique in the medical field?

Methods

To address the above questions, we conducted a systematic search of the literature published between 2003 and 2013 in major databases (PubMed/MEDLINE, the Cochrane Library, and ISI Web of Science). We searched for original papers, reviews, guidelines, and clinical trials using different keywords and phrases. The phrase "hyperspectral imaging" was combined with additional keywords and phrases: "cancer," "wound," "blood," "oxygen," "surgery," and "diabetic foot ulcers," "peripheral vascular disease," "dental caries," "traumatic skin injuries." We selected for this study (1) any article that reported the use of HSI in the medical field; (2) articles that present the device type, parameters, and sensitivity and specificity indices of this technique; (3) abstracts in English that present data on study design, sampling, and characteristics of the study group, outcomes, and performance of the technique; and (4) articles in referred journals. We excluded articles that (1) did not provide information that might be considered as answers to the questions above and (2) were published in a language other than English.

Results

Cancer Detection

Clinical applications of HSI in cancer detection are still limited. Seven studies published in the last decade reported promising results in detecting gastric cancer, tongue cancer, melanoma, prostate cancer (in mice), cancerous lung tissue (ex vivo, pathology slides), and cancerous lymph node tissue (ex vivo, pathology slides).

The performance of this technique in detecting gastric cancer was reported by Kiyotoki et al. (8). The study was carried out at the Yamaguchi University Hospital, Japan, on 16 gastroduodenal tumors removed by endoscopic resection or surgery from 14 patients using an HSI in the visible range (VIS, 400–800 nm). Ten samples of normal mucosa and 10 samples of tumors for each case were investigated by HSI. The results of this study revealed that tumors can be clearly distinguished from normal mucosa with 78.8% sensitivity and 92.5% specificity. A similar study was conducted by Akbari et al. (9) on 10 human subjects with gastric cancer. A total of 101 hyperspectral images of the resected stomach were acquired from all human subjects (after total gastrectomy) with an HSI in the infrared range (1,000–2,500 nm) and were correlated with the histopathology results. Using an advanced hyperspectral image processing technique, the authors reported a sensitivity of 93% and specificity of 91%. Comparing these results with those obtained by Kiyotoki et al. (8) from hyperspectral image analysis in the VIS range, using an infrared hyperspectral imaging system with a suitable image processing technique, the sensitivity of the HSI technique can be increased but not its specificity.

Outstanding results of the HSI technique in tongue tumor detection were also recorded. The study carried out by Liu et al. (10) on 34 tongue tumors using an acousto-optic tunable filter with a wavelength range of 600–1,000 nm and a spectral adapter showed that a recognition rate of 96.5% can be achieved using the HSI technique together with a classification algorithm based on sparse representation to distinguish between tumors and normal tissues. Based on these experimental results, the authors concluded that HSI can be considered a new method for diagnosing tongue tumors.

The HSI technique has proven to have great potential in the early detection of melanoma as reported by Nagaoka et al. (11, 12). The first study (11) was carried out on five melanomas, one Spitz nevus, 10 seborrheic keratoses, three basal cell carcinomas, and nine melanocytic nevi using a hyperspectral melanoma screening system and melanoma discrimination index derived from hyperspectral data in the VIS-near infrared (NIR) wavelength range. The results of this study revealed that by using this objective discrimination index, the melanoma could be discriminated from nonmelanoma with a sensitivity of 90% and a specificity of 84%. The study was conducted on only 20 cases (including 5 cases of melanoma) and further studies are needed to confirm these results. In the second study, Nagaoka et al. (12) applied the same hyperspectral melanoma screening system and melanoma discrimination index in order to discriminate the acral lentiginous melanoma from acral nevi. Thirteen cases of lentiginous melanoma and seven cases of acral nevi were included in this study. In this case, the method discriminated lentiginous melanoma from acral nevi with high sensitivity and specificity indices of 92 and 86%, respectively.

The possibility of using HSI for detection of prostate cancer was investigated in 2012 by Akbar et al. (13), and this is in fact the only study in this field. The research was performed both in vitro (on pathology slides of the prostate obtained from four patients) and in vivo (on 11 male nude mice, 9 of which had human prostate tumors transplanted on their flanks). Two hyperspectral imaging systems were used: an in vivo imaging system (450–950 nm) for animal scans and a microscopic imaging system (420–720 nm) for scanning pathology slides. A least squares support vector machine classifier was used to classify cancer tissue in animals and on pathology slides. The results showed that the sensitivity and specificity of the hyperspectral image classification method used for the detection of prostate cancer tissue in tumor-bearing mice were respectively $92.8 \pm 2.0\%$ and $96.9 \pm 1.3\%$. These preliminary results demonstrate that HSI together with appropriate methods of processing and analysis of hyperspectral images can be used in prostate cancer detection. In 2012 Akbari et al. (14) also proposed a novel macroscopic hyperspectral method for the detection of cancer metastasis. This is the first study on the use of hyperspectral imaging for cancer detection in pathology slides. The metastatic cancer was studied in lymph nodes and lungs. The method was evaluated on data sets of three slides of normal lung tissue, three slides of cancerous lung tissue, three slides of normal lymph node tissue, and three slides of cancerous lymph node tissue. The pathology slides were imaged using a hyperspectral imaging system in the VIS-NIR range (450–950 nm) and were classified using a support vector machine classifier. The results were evaluated in comparison with pathology reports. The results proved that the proposed method could detect metastatic cancer with high specificity and sensitivity of 97.7 and 92.6% in lung histological slides and 98.3 and 96.2% in lymph node slides. Given the outstanding performance of this method, the authors determined that the investigated method may be able to help pathologists to evaluate many histologic slides in a short period of time.

The results reported in these studies by only four groups of researchers seem to be promising, but more research is needed to confirm their value. Though in vivo studies draw attention to HIS as a new method to evaluate the extent of tumors or their malignancy that could help the surgeon in his approach, we believe that pathology slide evaluation with HSI is still to be tested, as long as classical pathological diagnosis is the best method and HSI does not seem to bring any advantages in terms of time or reliability.

Assessment of Diabetic Foot Ulcers

Foot ulceration is a serious complication of diabetes, and the development of new assessment techniques for management of the diabetic foot is a constant concern for researchers in the field. In recent years, some researchers have tested the ability of HSI to quantify tissue oxygenation (oxyhemoglobin and deoxyhemoglobin) and predict ulcer formation and healing on diabetic feet. One of the first clinical studies was conducted in 2007 by Khaodhiar et al. (15) on 37 patients (10 patients with 21 foot ulcer sites, 13 patients without ulcers, and 14 nondiabetic controls). All patients were investigated using HSI up to four times over a 6-month period. Hyperspectral tissue oxygenation (oxyhemoglobin and deoxyhemoglobin) measurements performed at or near the ulcer area and on the upper extremity and the lower extremity distant from the ulcer revealed changes in tissues immediately surrounding the ulcer that healed compared to ulcers that did not heal. Starting from these results, the authors developed an ulcer-healing prediction index based on the oxyhemoglobin and deoxyhemoglobin concentrations near the ulcer site that can be used to distinguish the ulcers that would heal from ulcers that would not heal. The sensitivity and specificity of the HSI technique in predicting healing, based on the images taken at the first visit, were 93 and 86%, respectively. These results demonstrated for the first time that HSI could be useful for foot ulceration management. A similar study was performed by Nouvong et al. (16) in 2009. Superficial tissue oxyhemoglobin and deoxyhemoglobin were measured from intact tissue bordering the ulcer using HSI in 66 patients with type 1 and type 2 diabetes. Healing potential was assessed using a healing index derived from oxy- and deoxyhemoglobin values. Based on this healing index, sensitivity and specificity of 80 and 74%, respectively, were obtained. These results indicate that HSI might be used to predict the healing of diabetic foot ulcers. More recent, Yudovsky et al. (17) described how HSI can be used to predict ulcer formation and healing in the diabetic foot. The authors presented two methods of analysis dedicated to hyperspectral measurements. One method (based on the modified Beer-Lambert law) was proposed to produce a map of oxyhemoglobin and deoxyhemoglobin concentrations in the dermis of the foot and the other method (based on a two-layer optical skin model) can be used to extract information not only about oxyhemoglobin and deoxihemoglobin concentrations but also about epidermal thickness and melanin concentration along with skin scattering properties. Using these methods, the changes in the diabetic foot can be detected and the ulceration etiopathogeny can be better understood. One year later, the ability of HSI to assess the risk of developing diabetic foot ulcers was investigated by Yudovsky et al. (18) in another study. The authors analyzed a set of hyperspectral data selected from those gathered by Nouvong et al. (16). These data from 21 affected sites were collected, on average, 58 days before the ulcer was first observed at the site and were retrospectively analyzed. An ulcer prediction index was developed and an image processing algorithm was implemented. The sensitivity and specificity of this algorithm to predict the risk of ulceration were determined as 95 and 80%, respectively. In addition, the authors demonstrated that HSI has the ability to identify ischemic and inflammatory complications before they are visible during a clinical examination. All of these advantages make the HSI technique useful in diabetes care, providing necessary information for treatment and prevention of complications.

HSI can be also used to measure the epidermal thickness for early prediction of diabetic foot ulcer formation as reported by Yudovsky et al. (19) in 2011. The study was performed on the feet of two diabetic patients before, during, and after they developed foot ulcers. The results of this study showed that a thickening of the epidermis and a callus formation appeared in preulcerous areas. The callus was seen to recede as the ulcer healed. The decrease in local epidermal thickness was associated with an increase in oxyhemoglobin concentration around the ulcer as it healed and closed. These results can be used to develop a methodology for early prediction of diabetic foot ulceration with practical applications in clinical settings.

All of the studies presented above show that HSI is a promising technique for the detection and care of diabetic foot wounds. First, it is a noninvasive and noncontact method. In addition, no effort or special preparation is required on the part of the patient prior to imaging. Finally, hyperspectral imaging provides, in one acquisition, high-spatial-resolution spectroscopy data over a larger portion of the sole of the foot. The method proves to be better than clinical examination, not only in predicting ulcer healing but also in pointing out the areas that need attention prior to ulcer formation.

Assessing Perfusion and Tissue Oxygenation in Various Pathological Vascular Conditions

HSI was tested as a method for assessing tissue perfusion in order to establish a pattern that can characterize peripheral vascular disease or other pathological conditions that can affect blood distribution. Chin et al. (20) and Johnson et al. (21) showed that HSI can be a reliable tool in assessing and classifying peripheral vascular disease or monitoring revascularized affected limbs. Both studies were designed using large groups of patients in well-established medical facilities and with good control using proven diagnostic tests (Doppler ultrasound, arteriogram), demonstrating a sound correlation of results. It is important to point out that both studies showed that the deoxyhemoglobin level measured with HSI is the most significant parameter in evaluating the amplitude of vascular disease or the effectiveness of surgery, whereas oxyhemoglobin has no diagnostic value. Therefore, future studies should take into account deoxyhemoglobin measurements, possibly in association with oxygen saturation readings.

An experimental acute peripheral ischemia model was designed by Neville and Gupta (22) in healthy individuals to test HSI as an assessment method. A combination of deoxyhemoglobin, oxyhemoglobin, and oxygen saturation measurements was used to establish a normal pattern followed by testing in experimental pathological conditions (induced acute ischemia using an inflatable cuff). Though the value of the interpretation methodology was proven, it still needs some correlation with classical clinical and paraclinical evaluations. Establishing which of the measured variables has the most important value might be useful, mainly because studies of chronic peripheral ischemia have pointed out that oxyhemoglobin measurements are inaccurate (20, 21).

Landeberg et al. (23) reported a complex analytical interpretation of hyperspectral images using principal component analysis, spectral angle mapping, and mixture-tuned matched filtering in order to establish a reliable method to identify skin changes in smoking versus nonsmoking individuals. Changes in skin vascularization can be assessed using depth resolution hyperspectral images, but the interpretation is rather complicated due to modulation of the chromospheres spectra by the optical properties of overlying tissue, therefore requiring the use of a combination of mathematical algorithms.

Klaessens et al. (24) compared the following imaging systems for assessing blood perfusion and oxygenation levels over time: two imaging systems consisting of a white broadband light source and a CCD camera in combination with a liquid crystal tunable filter, one in the VIS range (420–730 nm) and the other in the VIS-NIR range (650–1100 nm), and a CCD camera in combination with a software-controlled hyperspectral light source (a panel with 600 light-emitting diodes divided into 17 spectral groups in the spectral range 370–880 nm) so that specific spectral distributions can be generated at high repetition rate (>1,000 Hz) and a standard infrared thermal camera. A rather wide array of clinical applications was investigated, including tumor demarcation, early inflammation, effectiveness of peripheral nerve block anesthesia, and localization of epileptic seizure. The study showed that relative changes in oxygenation and temperature could be clearly observed in good correlation with the physiological condition, and the algorithms and data collection/processing can be optimized to enable a real-time diagnostic technique.

Along with studies concerning diabetic foot ulcers (see previous subsection), the articles cited in this section show that HSI can be a reliable method in assessing vascular input in peripheral tissues. They are not intended (so far) to replace the classical methods (arteriograms, Doppler ultrasound, pulse oximetry), but they seem to be a useful tool in helping clinicians to provide the best treatment to patients with peripheral vascular disease, whether chronic or acute.

Visualization of Organs and Tissues during Surgery

Surgery is a medical specialty that investigates and/or treats some pathological conditions and helps to improve bodily function using the most invasive tools available to medicine. Any surgical procedure presents some risks to the patient's health and therefore require high concentration and care. The success of surgical procedures depends on both amenities of the operating rooms and the surgeon's performance, especially related to hand–eye coordination. Visibility during surgery (field of view, contrast between the target and surrounding tissue, and view beneath the surface) is also very important, especially when making intraoperative decisions. All of these aspects have been investigated over time and various intraoperative imaging technologies to expand visibility have been developed. The most important of these are magnetic resonance imaging, computed tomography, and fluorescence imaging techniques. Development of new and reliable imaging technologies to assist the surgeon in making the right decision is a continuous field of research.

HSI is one a new approach proposed by some researchers as a possible intraoperative visualization method for residual tumor identification, bile duct visualization, and tissue oxygenation assessment. In 2007, Panasyuk et al. (25) reported the first results on the use of HSI in operating rooms in order to distinguish tumors from normal tissue. The study was performed on 56 rats using an imaging workstation that allowed both microscopic visualization and HSI of the operating field (spectral domain: 450–700 nm, 10-nm increments). Hyperspectral image data were acquired from the animals before and after partial and complete resections. Resected tissues were evaluated both by HSI and by pathological examination. The results demonstrated that different types of tissue (tumor, blood vessels, muscle, and connective tissue) could be clearly identified and differentiated using HSI. The HSI sensitivity and specificity indices for detection of residual tumor was determined to be 89 and 94% respectively; lower values of 85 and 92%, respectively, were recorded for pathological examination of the tumor bed. These results demonstrated that HSI might be used for the identification of small residual tumors in a tumor resection bed and the establishment of the areas that require more extensive resection.

To significantly enhance intraoperative biliary imaging, in 2008 Zuzak et al. (26) built a near-infrared hyperspectral imaging system that allows to surgeons to see through the hepatoduodenal ligament and detect the anteriorly placed biliary system without the need to dissect the cystic duct. This system was tested on porcine. The analysis of hyperspectral images of different porcine biliary structures revealed that the reflectance spectra of the common duct shows two main spectral characteristics situated at 930 nm (lipid) and 970 nm (water), and three other important maxima (760 nm: deoxyhemoglobin; 800 nm: oxyhemoglobin; 970 nm: water) were identified in the absorption spectra of venous structures. The absorption spectra of arterial vessels presented two main peaks at 800 and 970 nm (considered to be due to the presence of oxyhemoglobin and water). The authors showed that the chemical properties of tissues could be determined without the need for dissection using HSI.

Obtaining information about tissue oxygenation during surgical procedures would be particularly useful in a number of clinical situations, as noted in another study by Zuzak et al. (27). In this study, the authors reported the use of a new HSI with active spectral illumination for real-time visualization of the changes in tissue oxygenation that appear during kidney surgery. The hyperspectral images acquired on kidneys of four live pigs before, during, and after renal vascular occlusion revealed that a significant decrease (64.73 $\pm$ 1.5%) in the oxygenation of hemoglobin within 30 s of renal arterial occlusion may occur. These early results are encouraging and provide a basis for future development of new hyperspectral systems and methods for processing and analysis of hyperspectral images with important significance in surgical intervention monitoring.

Encouraging results were also reported by Akbari et al. (28) on the use of HSI for the detection of intestinal ischemia during surgery. The ischemic conditions were simulated by clamping the vessels supplying an intestinal segment of a pig and the hyperspectral images were acquired with two cameras, one VIS-NIR camera (400–1,000 nm) and one infrared camera (900–1,700 nm). The results showed that a clear distinction can be made between normal and ischemic intestines in a key wavelength range.

The possibility of using the HSI technique to monitor tissue oxygenation during porcine partial nephrectomy was recently evaluated by Best et al. (29). The study was conducted on 14 pigs with a solitary kidney that underwent open partial nephrectomy with warm ischemia. The hyperspectral images that were acquired at different moments (when the renal artery flow was reduced to 25, 10, and 0% of baseline for 60 min) provided information about the percentage of oxyhemoglobin at baseline, during ischemia, and during reperfusion. The role of incomplete renal artery occlusion was revealed. Favorable renal oxygenation profiles and a renoprotective role when 25% of the baseline renal artery flow is preserved were outlined. These results showed that the right intraoperative decisions can be made and protection of kidney function can be achieved by using HSI.

Though all the studies were performed on animals, the data that were gathered are encouraging, demonstrating that HSI can be a valuable tool in assessing organ vascular status or even the extent of tumor resection. A standardization of the method is needed in order to proceed to studies on humans.

Other Diseases Diagnosed by HSI

HSI has also been used to detect diseases such as dental caries and altered mucosa of the human larynx. Only two studies presented the applications of HSI in stomatology. A paper by Zakian et al. (30) described the use of HSI in the 1,000–2,500 nm spectral range for caries detection in 12 extracted teeth (premolars and molars) with different degrees of natural lesion. The authors suggested that based on the reflection spectra acquired using HSI the lesion severity can be quantified and an NIR caries score can be generated. The results of this study revealed that HSI can determine the presence of enamel lesions with a sensitivity of $>$99% and specificity of 87.5%, and for dentine lesions a sensitivity of 80% and specificity of $>$99% were recorded. The NIR hyperspectral imaging technique was also used by Usenik et al. (31) in 2011 to classify and visualize healthy and pathological dental tissues, including enamel, dentin, calculus, dentin caries, enamel caries, and demineralized areas. The study was performed on 12 extracted human teeth with different degrees of natural dental lesions. Two other methods (X-ray and digital color camera) were used to locate and classify dental tissues to obtain gold standard. The results demonstrated that a high correlation between the resulting classification and the gold standard (with a classification sensitivity and specificity of 85 and 97%, respectively) could be achieved. These high values of sensitivity and specificity make the NIR hyperspectral imaging a technique a potential tool for imaging of hard dental tissues. It is important to underline the fact that the cited studies were performed on extracted teeth and further research is needed to develop a hyperspectral imaging system that would work well in vivo.

Potential applicability of the hyperspectral classifications was also highlighted by Martin et al. (32) in the automatic detection of laryngeal disorders. The study was conducted on five cases of laryngeal disorders (two hemorrhagic polyps and three leukoplakia). Hyperspectral images acquired in the 390–680 nm spectral range were processed with unsupervised clustering (linear spectral unmixing) and spectral signatures were extracted from unlabeled cluster maps. This spectral information was used for subsequent supervised classification. The results revealed that abnormal laryngeal areas can be identified as single spectral clusters in all cases. Vocal cord polyps were identified with a sensitivity and specificity of 87.41 and 97.91%, respectively; for leukoplakia, detection was achieved with a sensitivity and specificity of 53.61 and 99.21%, respectively. Thus, laryngeal disorders could be identified using the hyperspectral hybrid method classification.

Discussion

Hyperspectral imaging is an emerging medical method that provides simultaneous spatial and spectral information about a tissue or organ and has great potential to improve the fields of medical diagnostics and clinical research. Although the HSI technique was introduced in the medical field relatively recently, it has already provided promising results in the detection of cancer, diabetic foot ulcers, and peripheral vascular disease and for the assessment of tissue blood oxygenation levels during surgery. In this article we presented some of the results based on a review of published literature relating to the effectiveness of HSI in diagnosis and evaluation of therapeutic methods. The results revealed that HSI provides accurate spatial and spectral information regarding the patient, tissue sample, or disease in more spectral ranges than visible, including infrared and ultraviolet spectral ranges, so that more information can be obtained. The extraction of useful information from the large amount of data contained in each medical hyperspectral image is needed, however. Different data processing methods have been proposed in the literature related to data calibration and correction, data compression, spectral dimensionality reduction, and data analysis (detection and classification) (9, 13–18, 20, 22, 23, 25, 26, 31, 32). It is only logical to assume that future studies will be able to find the best analytical method, but they might find that each application of HSI in a certain medical field has its own most reliable interpretation methodology.

Various hyperspectral imaging systems have been developed since AVIRIS (the Airborne Visible/Infrared Imaging Spectrometer), the National Aeronautic and Space Administration's first hyperspectral imaging system, was introduced in the late 1980s (33), and some of them are dedicated to medical applications (Table 1). When it comes to medical applications, the system should be easy to use, less time consuming than classical methods, and be adapted for use in special clinical settings like operating rooms. The areas of interest

Table 1
Hyperspectral imaging systems used in medical applications

Name	Manufacturer	Number of bands	Spectral range (nm)	Spectral resolution (nm)	Medical applications
CRi Maestro Systems	Caliper, Hopkinton, MA	100	450–950	5	Cancer detection
ImSpector Spectral Camera	Spectral Imaging Ltd., Oulu, Finland	238	1000–2500	6.29	Cancer detection
HSC1700 Hyperspectral Camera	Hokkaido Satellite Corp., Hokkaido, Japan	72	400–800	5.6	Cancer detection
HyperMed CombiVu-R System	HyperMed, Inc., Waltham, MA	20	500–600	5	Tissue oxygenation assessment
OxyVu	HyperMed, Inc., Burlington, MA	15	500–660	10.6	Tissue oxygenation assessment
HyperMed, Visible MHSI System	HyperMed, Inc., Watertown, MA	30	—	—	Tissue oxygenation assessment
HySpec	Norsk Elektro Optikk AS, Lorenskog, Norway	160	400–1000	3.75	Tissue oxygenation assessment

are wide thus far (as demonstrated by our review), and it is expected that specific systems will be developed for every clinical field of investigation.

It is obvious that it is difficult to set a standard for using the HSI technique in various medical applications. Each reviewed article had its own approach, mainly because these articles are addressed to so many fields of medicine. The authors believe that when dealing with a new technique the research has to be more specific. There are some areas of medical research where HSI proved to be of interest (tumor delimitation, evaluating perfusion in limbs or particular organs, detecting affected tissues). Further studies should focus on previous results and try to find a standard in finding the best technical system and an interpretation model. We stress that applications in the field of tissue perfusion, despite the clinical setup, are very promising, as long as oxygenation (measured in oxyhemoglobin, deoxyhemoglobin, and oxygen saturation levels) seems to be a future field for testing. In our opinion, there is much to study with regard to HSI in surgery, including finding the best technology that suits the particular conditions of the operating rooms, like respecting the aseptic rules and setting the system in an already crowded environment. HSI deals with objects that are within the investigator's sight, and its applications should focus on medical situations in which direct visualization of the investigated object is possible. Therefore, in vivo applications should focus on respecting this rule, which may be difficult in evaluating dental tissue, for example.

A complex multidisciplinary approach that includes medical practitioners, physicists, and software specialists will prove the method's value in the complex field of medicine.

Conclusions

In conclusion, HSI as a highly resolved means of imaging tissues can provide accurate spectral information related to the patient, tissue sample, or different disease conditions, but choosing the appropriate hyperspectral imaging system for each medical field, together with the most reliable hyperspectral image processing methods, should be the main goals of future studies, before hyperspectral imaging technique becomes a widely applicable evaluation method in medicine.

Acknowledgments

This work was financed by the Ministry of Education, Research, Youth and Sport by means of the Research Program No. PN II PCCA 184/2012.

References

1. Goetz, A.F.H., Vane, G., Solomon, J.E., and Rock, B.N. (1985) Imaging spectrometry for earth remote sensing. *Science*, 228 (4704): 1147–1153.
2. Daleab, L.M., Thewisa, A., Boudrya, C., Rotarb, I., Dardennec, P., Baetenc, V., and Fernández Piernac, J.A. (2013) Hyperspectral imaging applications in agriculture and agro-food product quality and safety control: A review. *Appl. Spectros. Rev.*, doi: 10.1080/05704928.2012.705800.
3. van der Meer, F.D., van der Werff, H.M.A., van Ruitenbeek, F.J.A., Hecker, C.A., Bakker, W.H., Noomen, M.F., van der Meijde, M., Carranza, E.J.M., de Smeth, J.B., and Woldai, T. (2012) Multi- and hyperspectral geologic remote sensing: A review. *International Journal of Applied Earth Observation and Geoinformation*, 14: 112–128.
4. Yuen, P.W.T. and Richardson, M. (2010) An introduction to hyperspectral imaging and its application for security, surveillance and target acquisition. *Imag. Sci. J.*, doi: 10.1179/174313110×12771950995716.

5. Hege, E.K., O'Connell, D., Johnson, W., Basty, S., and Dereniak, E.L. (2004) Hyperspectral imaging for astronomy and space surviellance. In *Proceedings of the SPIE 5159, Imaging Spectrometry IX*, doi: 10.1117/12.506426.
6. Holma, H., Hyvärinen, T., Mattila, A.J.J., and Kormano, I. (2012) Thermal hyperspectral chemical imaging. In *Proceedings of the SPIE 8374, Next-Generation Spectroscopic Technologies V*, doi: 10.1117/12.919294.
7. Shafri, H.Z.M., Taherzadeh, E., Shattri Mansor, S., and Ashurov, R. (2012) Hyperspectral remote sensing of urban areas: An overview of techniques and applications. *Res. J. Appl. Sci. Eng. Tech.*, 4 (11): 1557–1565.
8. Kiyotoki, S., Nishikawa, J., Okamoto, T., Hamabe, K., Saito, M., Goto, A., Fujita, Y., Hamamoto, Y., Takeuchi, Y., Satori, S., and Sakaida, I. (2013) New method for detection of gastric cancer by hyperspectral imaging: A pilot study. *J. Biomed. Optic.*, 18 (2): 026010-1–6.
9. Akbari, H., Uto, K., Kosugi, Y., Kojima, K., and Tanaka, N. (2011) Cancer detection using infrared hyperspectral Imaging. *Cancer Sci.*, doi: 10.1111/j.1349-7006.2011.01849.x
10. Liu, Z., Wang, H., and Li, Q. (2012) Tongue tumor detection in medical hyperspectral images. *Sensors*, doi: 10.3390/s120100162.
11. Nagaoka, T., Nakamura, A., Okutani, H., Kiyohara, Y., and Sota, T. (2012) A possible melanoma discrimination index based on hyperspectral data: A pilot study. *Skin Res. Tech.*, doi: 10.1111/j.1600-0846.2011.00571.x.
12. Nagaoka, T., Nakamura, A., Okutani, H., Kiyohara, Y., Koga, H., Saida, T., and Sota, T. (2013) Hyperspectroscopic screening of melanoma on acral volar skin. *Skin Res. Tech.*, doi: 10.1111/j.1600-0846.2012.00642.x.
13. Akbari, H., Halig, L.V., Schuster, D.M., Osunkoya, A., Master, V., Nieh, P.T., Chen, G.Z., and Fei, B. (2012) Hyperspectral imaging and quantitative analysis for prostate cancer detection. *J. Biomed. Optic.*, 17 (7): 076005-1–10.
14. Akbari, H., Halig, L.V., Hongzheng Zhang, H., Wang, D., Chen, Z.G., and Fei, B. (2012) Detection of cancer metastasis using a novel macroscopic hyperspectral method. In *Proceedings of the SPIE 8317*, *Biomedical Applications in Molecular, Structural, and Functional Imaging*, doi: 10.1117/12.912026
15. Khaodhiar, L., Dinh, T., Schomacker, K.T., Panasyuk, S.V., Freeman, J.E., Lew, R., Vo, T., Panasyuk, A.A., Lima, C., Giurini, J.M., Lyons, T.E., and Veves, A. (2007) The use of medical hyperspectral technology to evaluate microcirculatory changes in diabetic foot ulcers and predict clinical outcomes. *Diabetes Care*, 30 (4): 903–910.
16. Nouvong, A., Hoogwerf, B., Mohler, E., Davis, B., Tajaddini, A., and Medenilla, E. (2009) Evaluation of diabetic foot ulcer healing with hyperspectral imaging of oxyhemoglobin and deoxyhemoglobin. *Diabetes Care*, doi: 10.2337/dc08-2246.
17. Yudovsky, D., Nouvong, A., and Pilon, L. (2010) Hyperspectral imaging in diabetic foot wound care. *J. Diabetes Sci. Tech.*, 4 (5): 1099–1113.
18. Yudovsky, D., Nouvong, A., Schomacker, K., and Pilona, L. (2011) Assessing diabetic foot ulcer development risk with hyperspectral tissue oximetry. *J. Biomed. Optic.*, 16 (2): 026009-1–8.
19. Yudovsky, D., Nouvong, A., Schomacker, K., and Pilon, L. (2011) Monitoring temporal development and healing of diabetic foot ulceration using hyperspectral imaging. *J. Biophoton.*, doi: 10.1002/jbio.201000117.
20. Chin, J.A., Wang, E.C., and Kibbe, M.R. (2011) Evaluation of hyperspectral technology for assessing the presence and severity of peripheral artery disease. *J. Vasc. Surg.*, 4: 565–576. doi: 10.1016/j.jvs.2011.06.022.
21. Johnson, O.N., Slidell, M., Kreishman, P., Walcott, R., Scanlon, J., Arora, S., Macsata, R., and Sidawy, A.N. (2008) Hyperspectral imaging: An emerging technology as a potential novel adjunct in assessing peripheral perfusion deficits and success of lower extremity revascularizations. *J. Am. Coll. Surg.*, 207 (3, Suppl.): S114, doi: 10.1016/j.jamcollsurg.2008.06.295.
22. Neville, R. and Gupta, S. (2009) Establishment of normative perfusion values using hyperspectral tissue oxygenation mapping technology. *Vasc. Dis. Manag.*, 6 (6): 156–161.

23. Randeberg, L.L., Larsen, E.L.P., and Svaasand, L.O. (2009) Hyperspectral imaging of blood perfusion and chromophore distribution in skin. In *Proceedings of the SPIE 7161, Photonic Therapeutics and Diagnostics V*, doi: 10.1117/12.810027.
24. Klaessens, J.H.G.M., de Roode, R., Verdaasdonk, R.M., and Noordmans, H.J. (2011) Hyperspectral imaging system for imaging O2Hb and HHb concentration changes in tissue for various clinical application. In *Proceedings of the SPIE 7890, Advanced Biomedical and Clinical Diagnostic Systems IX*, doi: 10.1117/12.875110.
25. Panasyuk, S.V., Yang, S., Faller, D.V., Ngo, D., Lew, R.A., Freeman, J.E., and Rogers, A.E. (2007) Medical hyperspectral imaging to facilitate residual tumor identification during surgery. *Cancer Biol. Ther.*, 6 (3): 439–446.
26. Zuzak, K.J., Naik, S.C., Alexandrakis, G., Hawkins, D., Behbehani, K., and Livingston, E. (2008) Intraoperative bile duct visualization using near-infrared hyperspectral video imaging. *Am. J. Surg.*, doi: 10.1016/j.amjsurg.2007.05.044.
27. Zuzak, K.J.K.J., Francis, R.P.R.P., Wehner, E.F.E.F., Litorja, M.M., Cadeddu, J.A.J.A., and Livingston, E.H.E.H. (2011) Active DLP hyperspectral illumination: A noninvasive, in vivo, system characterization visualizing tissue oxygenation at near video rates. *Anal. Chem.*, 83 (19): 7424–7430.
28. Akbari, H., Kosugi, Y., Kojima, K., and Tanaka, N. (2010) Detection and analysis of the intestinal ischemia using visible and invisible hyperspectral imaging. *IEEE Trans. Biomed. Eng.*, 57 (8): 2011–2017.
29. Best, S.L.S.L., Thapa, A.A., Holzer, M.J.M.J., Jackson, N.N., Mir, S.A.S.A., Cadeddu, J.A.J.A., and Zuzak, K.J.K.J. (2011) Minimal arterial in-flow protects renal oxygenation and function during porcine partial nephrectomy: Confirmation by hyperspectral imaging. *Urology*, doi: 10.1016/j.urology.2011.06.029.
30. Zakian, C., Pretty, I., and Ellwood, R. (2009) Near-infrared hyperspectral imaging of teeth for dental caries detection. *J. Biomed. Optic.*, doi: 10.1117/1.3275480.
31. Usenik, P., Bürmen, M., Vrtovec, T., Fidler, A., Pernuš, F., and Likar, B. (2011) Automated classification and visualization of healthy and pathological dental tissues based on near-infrared hyper-spectral imaging. *Proceedings of the SPIE 7963, Medical Imaging: Computer-Aided Diagnosis*, doi: 10.1117/12.878264.
32. Martin, R., Thies, B., and Gerstner, A.O.H. (2012) Hyperspectral hybrid method classification for detecting altered mucosa of the human larynx. *Int. J. Health Geogr.*, 11: 21, doi: 10.1186/1476-072X-11-21.
33. Porter, W.M. and Enmark, H.T. (1988) A system overview of the Airborne Visible/Infrared Imaging Spectrometer (AVIRIS). *Proc. SPIE* 834: 22–31.