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Hyperspectral Imaging Applied to Medical Diagnoses and Food Safety

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ABSTRACT

This paper analyzes the feasibility and performance of HSI systems for medical diagnosis as well as for food safety. Illness prevention and early disease detection are key elements for maintaining good health. Health care practitioners worldwide rely on innovative electronic devices to accurately identify disease. Hyperspectral imaging (HSI) is an emerging technique that may provide a less invasive procedure than conventional diagnostic imaging. By analyzing reflected and fluorescent light applied to the human body, a HSI system serves as a diagnostic tool as well as a method for evaluating the effectiveness of applied therapies. The safe supply and production of food is also of paramount importance to public health illness prevention. Although this paper will focus on imaging and spectroscopy in food inspection procedures – the detection of contaminated food sources – to ensure food quality, HSI also shows promise in detecting pesticide levels in food production (agriculture.)

Keywords: Hyperspectral, Medical Imaging, Food Safety, Healthcare

1. INTRODUCTION

Cutting edge medical technology is vital for maintaining good health. Scientifically obtained information can aid health care professionals in early disease detection and swift diagnoses. Similarly, scientific knowledge about the safety of the food supply will prevent illness caused due to the consumption of unhealthy food. Consequently, electronic devices that provide scientific information are critical components in the medical and agricultural fields. In the medical community, they are used for disease detection, diagnoses, and evaluation of therapeutic methods. In the agricultural arena, electronics can support to food safety monitoring and inspection processes. This paper will examine the use of hyperspectral imaging (HSI) for both these applications. The potential positive impact of HSI has spurred much research by private companies and government agencies, with some joint efforts, including sharing of data and resources.

The organization of this paper is as follows:

1. Brief description of hyperspectral medical imaging
2. Medical applications – cancer detection, retinal imaging, tissue characterization
3. Food safety applications – food supply monitoring and inspection

2. HYPERSPECTRAL TECHNOLOGY & FLUORESCENCE

Hyperspectral remote sensing involves data collection in hundreds of bands, with each band or channel covering a narrow and contiguous portion of the electromagnetic spectrum. Hyperspectral sensing allows the image analyst to perform spectroscopy and evaluate reflectance, emittance, or fluorescence on each pixel (spatial element) of the image

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scene. HSI offers more information about the imaged target as it uses hundreds of spectral bands. For medical applications, HSI may provide an easier method of determining any abnormalities on the body, and thus better identify diseases.

Fluorescence occurs when an object illuminated with radiation of one wavelength emits radiation at a different wavelength. Due to their chemical structure, certain molecules, called fluorochromes or fluorophores, have the ability to absorb light of a shorter, higher energy wavelength and re-emit it as a longer, lower energy wavelength. This is termed as the Stokes shift, where the illuminated fluorochromes become excited into a higher, unstable energy state, which transitions to a lower state by the subsequent production and emission of photons of lower frequency. Fluorescence emission is characterized by intensity, wavelength (excitation and emission spectra), quantum yield, polarization, and lifetime. Fluorescence intensity is the most widely used parameter in analytical applications. For analysis, measured fluorescence is graphed using one axis to describe the spectral distribution of the illumination, and the other to show the spectra of emitted energy.

The fluorescence microscope is designed for detecting the light emanating from the fluorescent species – rather than from the light originally used to illuminate and excite the target. The object lens acts as condenser, which can provide optimum illumination with high numerical apertures. In designing the fluorescence microscope, a mercury lamp is used as the source of light as it can generate light that closely match the red, green, and blue dyes most commonly used by biologists. In the fluorescence microscope, the light passes through the heat filter and then through an excitation filter that can screen and block the incoming light except for the wavelength of the specific dye being the examined. The light will hit the specific mirror sitting directly above the objective lens called a dichroics filter. Dichroics are the mirrors that have a special coating which make them reflective to certain wavelength and transparent to other, longer wavelength light. If the fluorescence light becomes an excitation light, it will be corrected by the object and pass through the dichroic. Then the light goes through a third emission or barrier that will absorb the light. The light will then pass to a last filter ensuring that the excitation light does not have a contributing effect on the final image.

Traditional microscopic imaging involves examining stained histology samples with a three-color (RGB) camera. However, this does not allow for multicolor medical molecular imaging because it is not possible to “unmix” more than one colored label if they overlap in one pixel. The other major biomedical imaging technique based on the principles of fluorescence utilizes the body’s natural-fluorescing agents to identify abnormal cell morphology. This method requires filter cubes (sets of excitation and emission filters with a matched dichroic mirror and a grayscale camera). Fluorescence-based studies also introduce novel fluorescing agents used for multiplexed imaging to detect hundreds and thousands of different fluorescent labels simultaneously. The main problem with this is autofluorescence, where unwanted emission of light by unstained tissue samples can obscure the detection of specific fluorescent labels. In addition, since fluorescence detection often involves fluorescent spillover from one channel to another, corrective measures are required. Finally, with the introduction of new fluorescent reagents for specific testing, there comes the need for the purchase of additional filters.

Research continues for new optical methods for spectral discrimination combined with powerful software approaches (accurate algorithm to produce spectral information in a specified frequency band with a specified resolution) to obtain more information than conventional color-based imaging approaches. Two types of HSI prototypes are of interest:

- Imaging spectrometer (including some interferometric device) coupled with a scene camera for relaying optics (illuminate and collect reflected light); and,
- Microscope-based imaging capable of collecting the complete emission spectrum from a microscope slide – includes hardware (microscope, camera, band-sequential filters, light source) and software techniques for measuring the amounts of individual labels, or “unmixing” (currently a trial of various methods including spectral similarity mapping, automated clustering algorithms in *n*-dimensions, defining endmembers, and principle component analysis).

For both techniques, the key is to determine abnormal cell changes (suspicious areas) in relation to normal cell development.

3. MEDICAL APPLICATIONS – EARLY DISEASE DETECTION

Disease prevention and early disease detection are both paramount to maintaining good health. If early detection is accurately determined, effective therapy can applied to avoid permanent damage. An application of hyperspectral analysis could provide early detection of various types of cancer or retinal disease. In addition, a portable hyperspectral imaging system could be used to test for infection or abnormalities in bodily fluids (blood, urine, semen) and to determine blood and oxygen levels in tissue, especially during surgery. Finally, it may be possible to determine dental disease by using hyperspectral technology. All of these applications require there to be images and hyperspectral signatures of healthy tissues and fluids.

3.1 Cancer detection

Cancer is the second leading cause of death in the United States. While the causes of specific cancers continue to be widely researched, medical professionals have long emphasized early detection as key to prevent irreversible infliction. Displasia/neoplasia presents with distinct molecular characteristics (including nuclear content and size), tissue characteristics (including epithelial thickness), and increased vascularity to the area (termed angiogenesis). Precancerous areas tend to have an increased metabolism, demand greater nutrition, and have larger blood flow than normal tissue. Tissue fluorescence and reflectance spectra are both useful for evaluating metabolic and structural changes associated with neoplasia. HSI technology may aid in the diagnoses of cancer of the breast, cervix, and skin.

Cervical cancer. Causal factors for cervical cancer (known also as cervical intraepithelial neoplasia [CIN]) may include carcinogens, multiple cell mutations, viruses, and multiple causal factors. The human papillomavirus (HPV) is an identified risk factor for CIN. In the United States, over $6 billion is spent annually in the evaluation and treatment of low-grade precursor lesions, and our resources are also spent on the evaluation and treatment of lesions not likely to progress to cancer. (Richards-Kortum, 2000) The Papanicolaou (Pap) smear is the current standard approach for annual testing. Should this test turn out to be positive, the patient would then undergo a colposcopy, and finally, a biopsy to study the abnormal cells.

Optic technology that is based upon biochemistry and structure is ideal for diagnosing CIN. With sufficient spatial resolution, spectral imaging can reveal the increased vascularity in subsurface vessels of the cervix that contain hemoglobin (which has a high absorption coefficient compared to other tissue constituents) often found in cases of cervical cancer. Also associated with cervical cancer is an abnormality in the scattering of (abnormal) cells in the epithelium. These biomarkers allow for the use of optical spectroscopy for screening for histo-chemical features of this disease. From one study, it was determined that "if spectra are obtained at multiple excitation wavelengths, good discrimination between normal cervix and pre-cancer can be achieved." (Richards-Kortum, 2000) Another, more recent study provided evidence that a hyperspectral system "detected cervical cancer precursors at a rate greater than that obtained by a simultaneously collected Pap smear." (Ferris, 2001) Although this study used a small test sample that scanned only the ectocervix, rather than the endocervix as well, the researchers showed that spectral sensing has the potential to discern grade of disease.

A spectral test for CIN includes UV illumination to record the intensities of fluorescence emission and white light illumination to record reflected light in the visible light range. During trials, this data is then compared to colposcopic results and histopathologic reports. From this, it is possible to determine normal squamous epithelium and identify biopsy locations. In clinical trials, HSI can be evaluated in comparison to traditional tests that include video image and biopsies. For effective results as compared to traditional methods, HSI would need to discriminate pathological grade (e.g. CIN-2); however, this requires much more testing and evaluation.

Breast Cancer. Recent study has led to the notion that the HSI classification technique holds much promise in detecting breast cancer cells. Traditional breast cancer screening tests (mammography) use X-rays to visualize the internal structure of the breast. The use of a hyperspectral sensor may image molecular properties of precancerous cells, namely, increased blood (and thus heat) to the area. Since HSI is limited by the user's ability to pull relevant information out of the enormous quantity of data it provides, the development of an unsupervised algorithm based on multiple spectral data per pixel may be used to classify infrared heat radiated from abnormally reproducing breast cancer cells.

Although HSI technology may aid in cancer detection, it is important to note that, at this time, this technology should be used in conjunction with traditional diagnostic methods. HSI may also serve to determine the spread of cancerous cells and guide doctors to spectroscopy-directed biopsies.

3.2 Retinal imaging

By using optical imaging methods, ophthalmologists can gain an understanding of pathological changes (in morphology, pattern, and color) of the retina. Hyperspectral imaging of the eye could be a promising diagnostic aid in this effort. The photon-sensing role of the eye implies optical access to the retina over a wide band of wavelengths. (Cohen, 1999) A normal retina presents a reddish appearance that is due to the presence of chromophores hemoglobin and melanin that absorb more strongly at shorter wavelengths. An abnormal retina presents differently because the change in physiology results in altering the reflectivity spectrum, as seen in diabetic retinopathy (hemorrhage – excessive hemoglobin concentrations) and in macular degeneration (abnormal protein or lipid concentrations).

In order for a hyperspectral imaging system to capture wavelength scattering and absorption properties of the various components of the eye, an external illumination from a filtered tungsten lamp is required. Due to the turbidity in the retina and the choroids (an optically dense complex of blood vessels), and the scattering property of the sclera (the “white” structure of the eye), photons migrate between the elements. A hyperspectral imaging technique may capture the wavelength reflectivity of the retina and the blood vessels. Since retinal disease generally occurs above or below the absorbing melanin layer, which rests within the retina, a hyperspectral image of the retina could reveal abnormalities. A healthy image of the retina can be compared to test intensities at various wavelengths. Abnormal spectral signatures could signify surface lesions, unbalanced melanin concentration, and a potentially harmful hemoglobin concentration.

3.3 Tissue characterization

Current approaches for assessing blood flow through tissue (tissue perfusion) include oximetry which monitors the visible and near-infrared spectral properties of blood by recording variations in the percentages of oxygen saturation of hemoglobin. For example, the concentrations of oxyhemoglobin (HbO_2) and deoxyheoglobin (deoxy-Hb) in the tissue can be measured, and reveal potentially ischemic (oxygen depleted) tissue. Oximetry, however, only measures oxygen saturation at either one or several sample points. Therefore, visible reflectance hyperspectral imaging of body tissue could be of great utility in determining the tissue perfusion and reperfusion. Moreover, this could be beneficial during and after surgery and/or during diagnostic procedures to determine healthy tissue perfusion or ischemic tissue.

Zuzak, et al. are conducting this type of imaging system to collect spectroscopic data from a large array detector at multiple, continuous wavelengths at narrow spectral bandwidths. From this, each pixel allows a determination of a molecular spectrum from which the characteristic state of the tissue is assessed. Data on the visible reflectance spectra of HbO_2 and deoxy-Hb from skin tissue indicate that radiation, which is re-emitted from the dermal layer, penetrates typically 1-2 mm below the skin surface. (Zuzak, 2002) The experiments include baseline hyperspectral images of a subject’s hand, at rest, followed by occlusion by a blood pressure cuff, followed by reperfusion measurements. The visible reflectance imaging system easily performs the spatial and temporal measurements required for assessing the changes in the percentages of HbO_2 across a skin area during the various phases of first ischemia and then the subsequent reactive hyperemia, which occurs during reperfusion. (Zuzak, 2002) As tissue type is distinguished by their absorption of light, healthy blood flow to an area will give a specific spectral signature, whereas, unhealthy flow will be noticed by the health care professional. This experiment showed health care practitioner could take an image of a part of the anatomy with submillimeter spatial resolution while visualizing chemical changes at the molecular level. Special attention can then be found; for example, precancerous areas tend to have an increased metabolism and larger blood flow than normal tissue, and appear as different colors. The HSI technology “sees” over 300 separate colors compared to three colors (red/blue/green) captured by ordinary cameras, and thus unhealthy tissue perfusion with specific spectra can be a signal for something more serious.

4. ILLNESS PREVENTION – FOOD SAFETY

The Centers for Disease Control and Prevention (CDC) estimates a high incidence of foodborne illness in the United States: approximately 5,000 deaths, 325,000 hospitalizations, and 76 million illnesses annually. (Taylor, 2001) Public health officials emphasize safe handling and processing of our nations food supply as key elements in preventing food-related illness. The U.S. Department of Agriculture (USDA) has a statutory mandate to inspect every carcass passing through slaughter establishments and to inspect every meat and poultry processing plant every day. (Taylor, 2001) However, the USDA and the Food and Drug Administration (FDA) we believe, are unable to meet this challenge at this time due to differentiated mandate policies and skewed budgets and staff.

Hyperspectral imaging could be used at critical control points of food processing to inspect for potential contaminants of the supply of poultry, produce, and grains. HSI technology could contribute significantly to risk reduction goals in food safety by effectively detecting microbial pathogens such as *Salmonella* and *Escherichia Coli* O157:H7 (*E.Coli*). Analysts could find the wavelengths best suited to spotting fecal contamination or cuts and bruises on produce.

Salmonella is a gram negative, facultative anaerobic, short rod organism, residing in intestines of human and animal populations. Raw poultry products are noted for harboring *Salmonella*. When ingested in large concentrations (1 million *Salmonella* per gram), the organism will cause *Salmonellosis*, a disease where symptoms include nausea, vomiting, headache, diarrhea, and fever. It can be fatal to the very young, elderly, or immunocompromised individuals. To prevent *Salmonella* food poisoning it is important to refrigerate food appropriately, cook food properly, and prevent contamination of raw food by infected food handlers.

Current strategies to detect of *Salmonella* in food samples include an immuno-assay method and the use of polymerase chain reaction technology. The conventional method is a standard plate count: 25 gm of sample were inoculated into 225 milliliters of buffered peptone water (BPW) broth and inoculated overnight at 37^{o}C. Selective enrichments were selenite-cystine (SC) broth (10 ml into 100 ml SC) and Rappaport Vassiliadis (RV) broth (100 µl into 10 ml RV). Plating on Xylose-lysine-Desoxycholate (XLD) and brilliant green agar (BGA) media presumptively identified *salmonella* and representative colonies were confirmed as *Salmonella* by classical biochemical and serological tests.

Recently, apple juice contaminated with *E. coli* has caused major illness outbreaks. *E.coli* can get into the human body by drinking of unpasteurized apple juice or by consumption of contaminated apple skin. When apples are mashed, *E.coli* is also the part of the mash and juice, and if pasteurized, *E.coli* will be killed. However, 2 percent of the fruit and vegetable juices sold in this country are unpasteurized, and that 2 percent accounts for an estimated 16,000 to 48,000 people. (Comis 2002) HSI technology offers a new method for bacteria and virus detection. Analysts could determine the optimal wavelengths to identify areas of fecal contamination on produce.

Food products possess high quality requirements for both inspection purposes and for safe consumption. Hyperspectral analysis can measure the reflectance and fluorescence from the visible range to the near infrared range. According to Kim et al (2000), the optimal spectral range is from 490-930 nm with spectral resolution of approximately 10 nm (full width at half maximum) and spatial resolution better than 1 mm. Ongoing research efforts show the effectiveness of HSI in detecting disease-causing organisms in our food supply[5].

In addition, HSI can also spot contamination from ingesta (partially digested food from the ruptured crops of chicken carcasses). A HSI system for detecting the fecal and ingesta consists of a camera with prism-grating-prism spectrograph, fiber optic line, lighting, motorized lens control, and hyperspectral image software. Park (2001) showed a hyperspectral image process algorithm, specifically band ratio of dual wavelength (565/517) images and histogram stretching, were effective in identifying fecal matter and ingesta on chickens. As HSI can detect and identify microbial pathogens, dirt, fly specs, and fungi during food processing, proper removal and cleaning will further reduce the likelihood of cross contamination during processing.

In general, a hyperspectral imager can be valuable on the assembly line during the processing of a wide range of food products. For example, an HSI unit can be used to monitor for contaminants in natural raw materials of nutritional supplements. According the research by the Nutritional Business Journal in 2000, the U.S. nutrition industry (health and wellness) was valued at approximately $48 billion and was expected to grow 6.2% from 2001 to 2003; specifically, the U.S. dietary supplements industry was considered to be $17.7 billion in 2002.[6] Imaging spectroscopy could be used to

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[5] For more details on current techniques for evaluating food safety issues, we refer the reader to the Food Safety Program at The USDA Agricultural Research Service, available on the web at URL http://www.nps.ars.usda.gov
[6] For more information, we refer the reader to the web at URL www.nutritionbusiness.com

aid good manufacturing practices (GMPs) by employing the use a widely accessible, up-to-date spectral library containing signatures of contaminants. In this manner, hyperspectral technology can be used to further ensure the safe supply of vitamins, herbs, minerals, sports nutrition products, and other specialty supplements. A similar set-up (contaminant spectral signature database and a HSI system) can also be used in real-time to monitor organic foods that are laid out (i.e., presented in buffet-style). Foods that are presented in such a manner are highly susceptible to spoilage and contamination, and consequently, are the sources of many food-borne illnesses. Constant spectral monitoring can be a significant illness prevention technique by ensuring a safe supply of organic foods.

For realizing benefits in either of these applications, however, those in the geomatics industry need to cooperatively act on a number of unresolved issues, including[7]:

- User-friendly software for spectral analysis and the establishment of a web-based spectral library;
- Dissemination of spectral information – use of the Internet;
- Data handling and interpretation of exponentially growing spectral data collection – use of a universal clearinghouse with sturdy, but flexible scientific and administrative structures;
- Standards for spectral signatures – including metadata that gives information on sensor attributes, guidelines for including data in the library such that the database can be ubiquitously used for queries and software analysis for specific calculations; and,
- Establishing architecture of an open-access spectral database that will give value by providing better quality data (via competition and standards), allowing for addition and retrieval of data adequately stored data, and permitting applications across various fields with ease and credibility.

5. CONCLUSION

While medical imaging is essential to medical diagnoses, the development of an effective hyperspectral imaging system is still in its infant stages. Clinical tests will provide evidence for future applications in this area. Today, however, many in the medical industry can agree to potential benefits of hyperspectral imaging in the medical field, including:

- Potential for cost effective, non invasive, accurate diagnostic preventive tests
- Potential to support clinical judgment and provide targeted biopsies.
- Aid effective decision-making by medical professionals during diagnosing, follow-up (more specific) testing, therapy selection, & monitoring.

Before the use of HSI is widely accepted in the medical diagnostic field, there needs to be *in-vitro* (studies to determine optimal wavelengths for diagnosis) versus *in-vivo* comparison studies determining spectral imaging accuracy.

The application of an HSI system will, perhaps, be accelerated in the field of food safety. Public health officials realized benefits of spectral imaging in the food industry, including:

- Shorter detection times
- Acquisition of a unique spectra for bacteria, permitting for more accurate results
- Monitoring the production of a large quantity of foods

Regardless of which field sees the application of HSI technology first, data gathered, analyzed, and interpreted needs to be scientifically accurate to be of any value during decisions concerning illness potential and disease detection.

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[7] To learn more about the issues concerning spectral libraries, please review the 2001 article by R.B. Gomez entitled, *Spectral Library Issues in Hyperspectral Imaging Applications*.

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