LASER PROGRAM

L.1 Statistical pattern recognition based diagnostic algorithms for autofluorescence diagnosis of oral cancer

A successful use of autofluorescence spectroscopy for cancer diagnosis requires an accurate and fast diagnostic algorithm that can best quantify the subtle but significant spectral differences between normal and abnormal human tissue. Development of such algorithms comprises of two major steps: (i) extraction of prominent features from the observed spectra by reduction of the dimensionality of the measured spectral variables, and (ii) classification of the diagnostic features by using the stored spectral database from histopathologically characterized tissues.

We have recently explored use of several state-of-the-art statistical pattern recognition based approaches to optimize both these aspects of algorithm development. For feature extraction, we used nonlinear maximum representation and discrimination feature (MRDF) approach to dimensionally reduce the input spectral data. A set of nonlinear transforms (polynomial mapping) was used to ensure that the output nonlinear features for cancerous and normal tissue were statistically best separated from each other in the reduced dimensionality space. These MRDF features were used as input to a traditional nearest mean classifier for classification. The results obtained using MRDF approach were significantly better compared to those obtained by use of the linear features (extracted using classical Principal Component Analysis (PCA) or Fisher's Linear discriminant (FLD)) as input to the same classifier [Lasers Surg. Med. 33, 48-56, 2003]. For supervised classification we have explored use of the theory of support vector machine (SVM). We developed a methodology that makes use of SVM for both feature extraction and classification jointly by integrating the newly developed recursive feature elimination (RFE) in the framework of SVM. This led to significantly improved classification results compared to that obtained when SVM was used in conjunction with features extracted using PCA. The integrated SVM-RFE approach was found to outperform the classification results yielded by FLD based algorithms. The best sensitivity and specificity values provided by the nonlinear SVM-RFE algorithm over the data sets investigated were 95% and 96% towards cancer for the training set data based on leave-one-out cross validation and 93% and 97% towards cancer for the independent validation set data [To appear in Journal of Biomedical Optics, 2005]. Though SVM-RFE algorithm provides very good diagnostic efficacy it has one limitation in that it cannot provide a quantitative estimate of the confidence with which a site is classified in a specific group (normal or malignant, in the present case). To address this important issue we have investigated the applicability of the recently formulated theory of relevance vector machine (RVM) for development of a probabilistic classification scheme. The RVM based algorithms showed diagnostic performance comparable to SVM. The use of RVM based algorithm would be very helpful in clinical setting where the cost of misclassification is asymmetric, that is one would want to ensure that virtually none of the malignant site is classified as normal even if ensuring this implies that a few of normal sites may get classified as malignant.

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L.2 Development of 60 Watt kinetically–enhanced copper vapor laser

Kinetically–enhanced high power copper vapor lasers (KE-CVLs) are the most recently developed CVL systems. The output power and efficiency increases by factor of 2-3, without any significant change in the design, circuit and total input power of the standard elemental copper vapor lasers. This is accomplished by operating the KE-CVL at higher rep-rate (9- 20 kHz) and using special buffer gas mixture consisting of HCl, hydrogen and neon in highly optimized proportions as per the system requirements [M.J. Withford, D.J.W. Brown, R.P. Mildren, R.J. Carman, G.D. Marshall, J.A. Piper, Progress in Quantum Electronics vol. 28, 2004, p165; *B. Singh, S. R. Daultabad, V. V. Subramanyam, A. Chakraborty*, Proc. National Laser Symposium, Jan. 2005, p115]

The presence of HCl ensures the favorable control of the electron density in the discharge mainly by the process of dissociative-attachment, thereby, enhancing the CVL

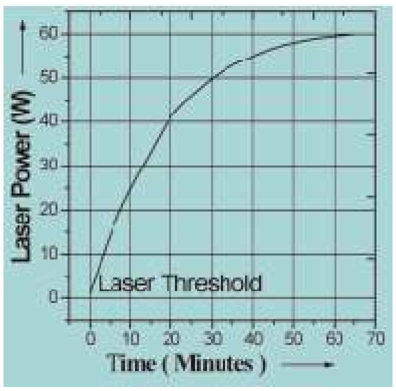

Fig L.2.1 *KE-CVL power buildup with time*

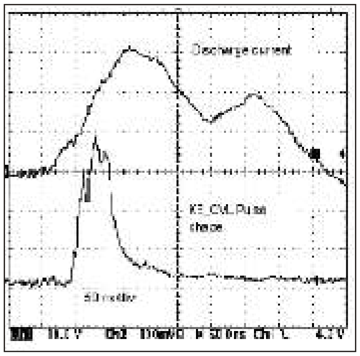

***Fig. L.2.2** Discharge current and laser pulse shapes*

performance dramatically. We have successfully demonstrated an indigenous kinetically–enhanced CVL system with 60-65 Watt power, based on these concepts and parameters. The laser was operated at ~ 9-10 kHz rep-rate at a total input power of about 5 kW with an overall electro-optic efficiency of about 1.25%. The laser output power buildup with time is fast and efficient as shown in fig.L.2.1. Also, the high efficiency of the CVL is maintained at low input power level of ~ 3kW. This gives an added option of operating the KE- CVL at low input power efficiently as per the need and application of the CVL beam. The KE-CVL pulses are longer in duration by 25% with better beam quality as compared to normal standard CVLs (fig.L.2.2)

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L.3 Depth resolved fluorescence measurement in layered turbid medium by polarized fluorescence spectroscopy

For epithelial tissue, it has been shown that the contrast in auto-fluorescence from malignant and nonmalignant sites depends strongly on the difference in depth distribution of endogenous fluorophores [Drezek et al, Photochem. Photobiol., 73, 636-641, 2001]. Therefore, depth resolved fluorescence measurements, which can decouple the epithelial and stromal (connective tissue) fluorescence, would help maximize the contrast between malignant and nonmalignant tissue sites and thus improve diagnosis. We have demonstrated that measurement of fluorescence polarized at different angles with respect to the linearly polarized excitation can be used to probe fluorophores located at different depths inside tissue. This arises because the fluorescence emitted from deeper layers of tissue gets more depolarized due to multiple scattering compared to that emitted from superficial layers.

The applicability of this approach was demonstrated using a two-layered tissue phantoms and resected tissue samples. The samples were illuminated by linearly polarized light (λ_{ex} = 440 nm) from a 450 Watt xenon lamp and polarized fluorescence spectra [$I^{fl}(\Delta\theta, \lambda)$] were recorded for varying angles ($\Delta\theta$) between the polarization axes of the analyzer with respect to the excitation polarizer. A synchronous scan with zero offset between the excitation and the emission monochromators was used to record polarized elastic scattering spectra [$I^{es}(\Delta\theta, \lambda)$].

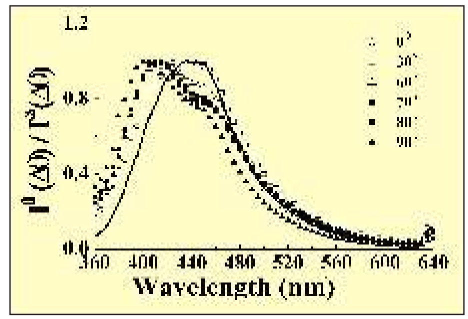

***Fig. L.3.1** Dependence on $\Delta\theta$ of the 340 nm excited elastic scattering normalized fluorescence spectra [$I_n^{fl}(\Delta\theta, \lambda) = I^{fl}(\Delta\theta, \lambda) / I^{es}(\Delta\theta, \lambda)$] from mice oral tissue sample.*

In fig.L.3.1, the dependence on $\Delta\theta$ of the 340 nm excited fluorescence spectra [$I_n^{fl}(\Delta\theta, \lambda)$] from an epithelial tissue resected from oral cavity of mice is displayed. In order to compensate for wavelength dependent propagation losses in fluorescence coming from deeper layers, the fluorescence was normalized with respect to the elastic scattering spectra [$I^{es}(\Delta\theta, \lambda)$] recorded under the same conditions. The difference spectra [$I_n^{fl}(\Delta\theta = 0^o, \lambda) - I_n^{fl}(\Delta\theta = 90^o, \lambda)$, displayed by solid line] and the normalized fluorescence spectra at smaller $\Delta\theta$ values ($\Delta\theta = 0^o, 30^0$) shows prominent peak around 440 nm that is a characteristic signature of NADH present in the superficial epithelial layer of tissue. Spectra recorded at larger $\Delta\theta$ show a prominent peak at ~ 400 nm that represents collagen and elastin present in the deeper connective tissue layer. [For more details: *N. Ghosh, S. K. Majumder, H. S. Patel and P. K. Gupta, Optics Letters, to appear in 30 (2005)*].

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L.4 X-ray bolometer for studies of laser produced plasmas

Absolute quantitative measurements of broad band (10 eV < $h\nu$ < 5 keV) X-ray fluence from pulsed plasma sources such as laser produced plasmas, Z-pinch plasmas etc. play an important role in using intense X-ray emission from these plasmas for applications in the indirect inertial confinement