Laser applications in medicine: Studies at Centre for Advanced Technology

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The article provides a brief overview of the work being carried out at Centre for Advanced Technology, Indore, on laser applications in medicine as well as on the development of medical laser systems.

LASERS are finding widespread applications in the field of medicine. A continuous improvement in medical laser systems and associated technologies is leading to a rapid growth in the range of laser applications in medicine. Lasers are not only being used for minimally invasive, ultraprecise surgical applications[1] but also for various photo-therapeutic modalities[2–4] and biomedical diagnostic applications[5–7].

The use of lasers in medicine is growing in our country also, driven by the realization that it can offer quality health care with reduced patient trauma and hospitalization time. A good example is the growing use of lasers in various ophthalmic procedures even by private practitioners in relatively smaller towns. Though the use of lasers in other surgical modalities is also picking up[8–12], the over all use of lasers in medicine in our country is still rather limited compared to developed countries. One major reason for this is the high cost of imported laser systems and the fact that often their maintenance and servicing proves to be very expensive and difficult. With a view to correcting this situation, development of medical laser systems was taken up at Centre for Advanced Technology (CAT), Indore, right at its inception in 1986. Later, work was also initiated to develop other laser applications relevant to medical problems specific to our country. For this purpose development of laser systems to pursue promising photo-therapeutic procedures like N_2 laser-based treatment of pulmonary tuberculosis was taken up. Development of laser spectroscopic methods for medical diagnosis and studies directed towards understanding laser photo-therapeutic effects have also been initiated at CAT. The progress made in these areas is briefly described in this article.

Development of medical laser systems

Surgical CO_2 laser system

The first medical laser unit developed at CAT was a continuous wave (CW) CO_2 laser system which happens to be the most widely used surgical laser system. A major reason for this is that the CO_2 laser radiation is strongly absorbed in water, the major constituent of all tissues. The CO_2 laser interaction is therefore not tissue-specific and the laser can be used as a general purpose surgical tool. Further, its small penetration depth (~ 15 μm) allows high precision and minimal thermal damage to the surrounding tissue.

The CO_2 surgical laser system developed at CAT is shown in Figure 1. The CO_2 laser output is coupled to an articulated arm to provide easy three-dimensional maneuverability of the beam. The system can provide CW output variable from a few mW to up to 30 W at the tip of the articulated arm. To suit different clinical needs the laser can also be operated in chopped mode (power output variable from few mW to 30 W and exposure times variable from 0.1 s to 1.0 s in steps) and superpulse mode (energy per pulse 20 mJ, pulse duration ~ 100 μs, repetition rate up to 500 Hz, and average power up to 10 W). The unit incorporates a He–Ne laser guide beam, in-built safety interlocks and other features comparable to

Figure 1. The surgical CO_2 laser system developed at CAT.

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imported units. In addition, some special features like an in-built water chiller unit have been added to make the system better suited for Indian working conditions. The first prototype of the surgical CO_2 laser system was supplied to Choithram Hospital and Research Centre (CHRC), Indore for clinical use in May 1990. Several improvements were carried out in the system, over the next two years, based on the feedback received from the surgeons using the laser system. The Production Unit at CAT is now making this system on a routine basis according to the demand from the users. Twelve units of the system have been supplied by it to several hospitals across the country at less than half the cost of an imported unit and are working satisfactorily. Over 1000 surgical procedures in ENT/gynecology have already been performed at CHRC using CAT built surgical CO_2 laser unit. In ENT, the laser is being used regularly for various ablative procedures, viz. tonsilar ablations, submucous fibrosis, laryngeal stenosis, leukoplakias, etc. Oral submucous fibrosis is very common in our country due to the consumption of tobacco and pan masala. In this condition the patient is not able to open his mouth fully (Figure 2). The laser treatment is carried out as an outpatient procedure and excellent results have been obtained[11]. The CO_2 laser is also being used at CHRC for treatment of snoring using Laser-Assisted Uvulopalatoplasty (LAUP), an OPD procedure done under local anesthesia. In gynecology, CO_2 laser is being used at CHRC for vaporization of cervical and vulvar intraepithelial neoplasia (CIN and VIN), and vulval dystrophy.

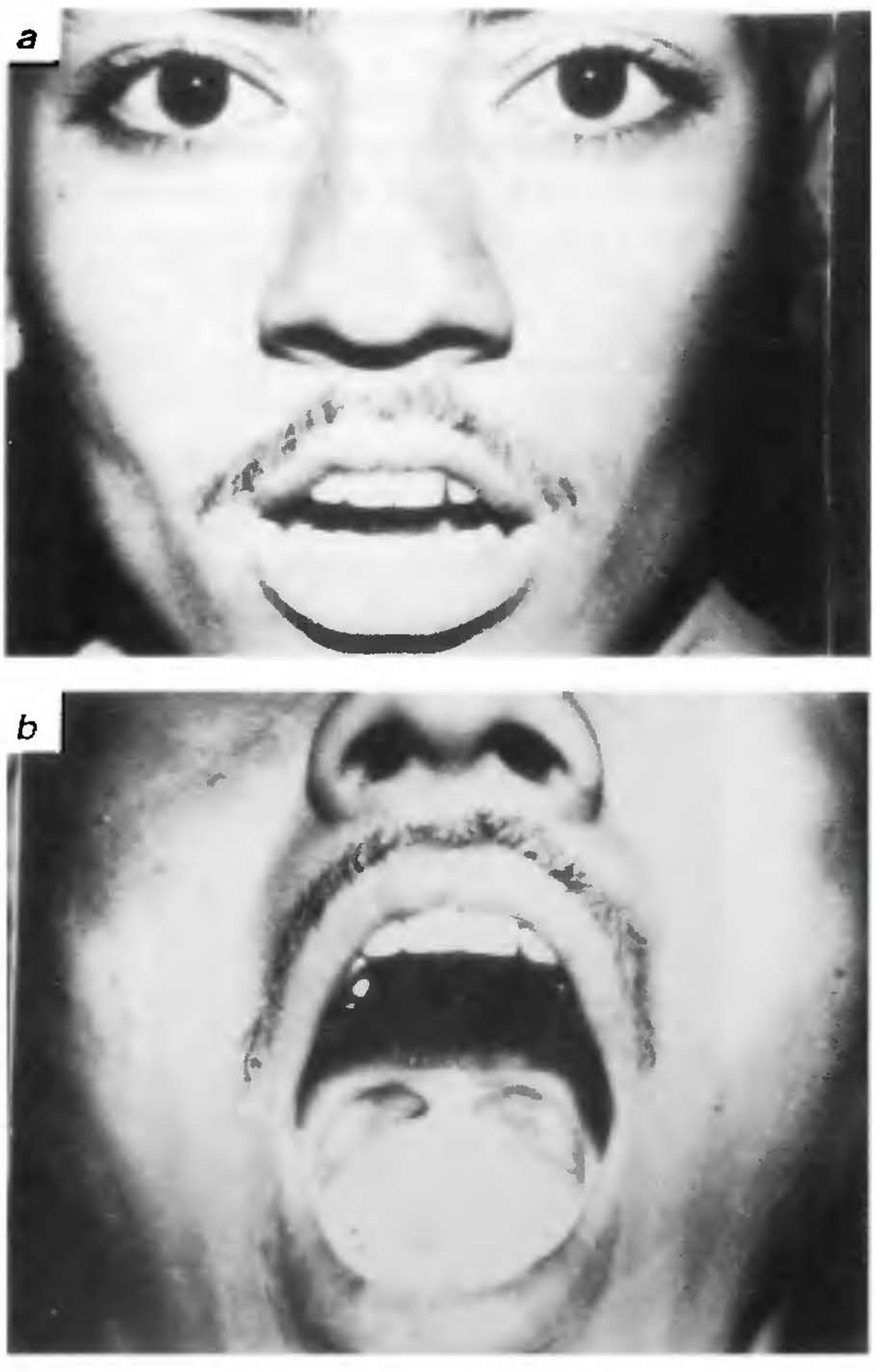

Figure 2. The use of surgical CO_2 laser for treatment of submucous fibrosis. *a*, Opening of mouth 1 cm only. *b*, Same patient after CO_2 laser surgery. He can now open his mouth fully.

N_2 laser systems

N_2 lasers (2–10 mW, 10–100 Hz) with fiber optic beam delivery have also been developed at CAT (Figure 3). These are in use at CHRC, M.G.M. Medical College and M.Y. Hospital, Indore for treatment of pulmonary tuberculosis. This treatment modality was pioneered by M. Eshankhanov *et al.* at Second Medical Academy, Tashkent[13]. The work was motivated by the work of Niels R. Finsen, a Danish physician and the winner of the 1903 Nobel Prize for medicine, who established the role of UV light in curing skin tuberculosis. The difficulty of taking the UV radiation inside the pulmonary tubercular cavity was solved by coupling the 337 nm N_2 laser output to a quartz optical fiber and inserting the fibre in the cavity. The procedure, which is carried out on an outpatient basis, is shown in Figure 4. A wide bore needle attached to a syringe filled with isotonic saline is introduced in the cavity directly through the chest wall (from behind) under local anesthesia. Entry of the needle into the cavity is confirmed by free flow of air in the syringe. The syringe is then disconnected and a quartz fibre carrying N_2 laser radiation is introduced through the lumen of the needle into the cavity. After irradiation for a fixed time, the fibre is withdrawn and the needle pulled

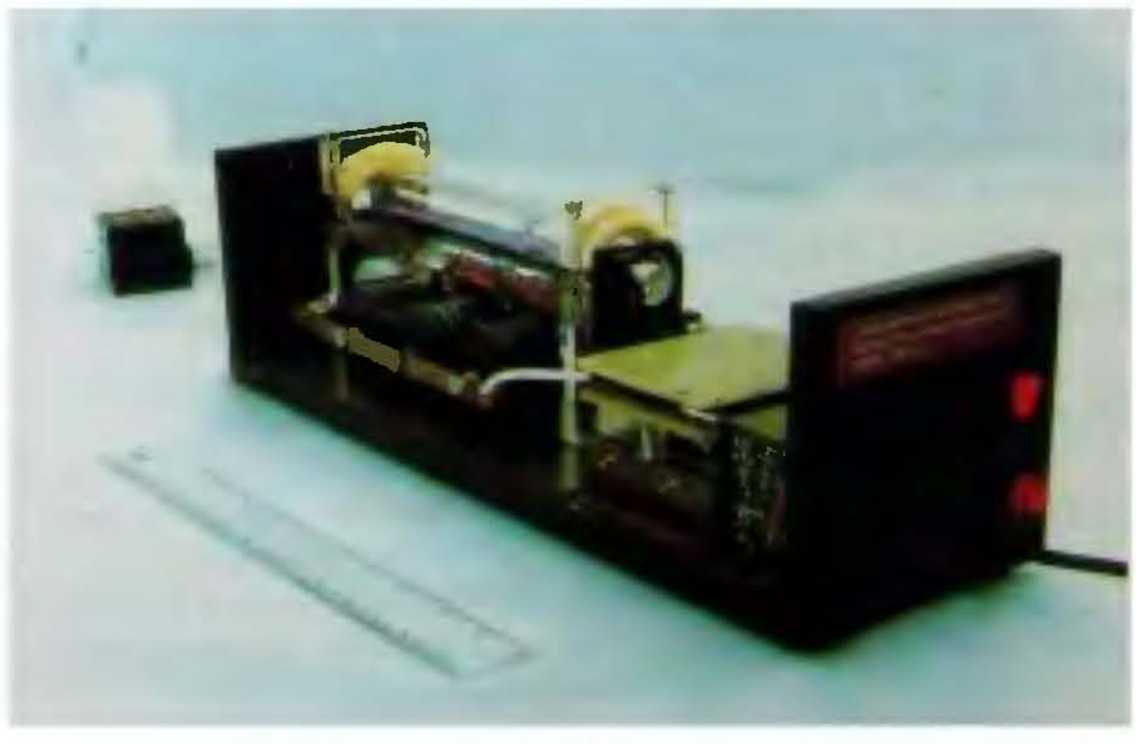

Figure 3. A sealed N_2 laser developed at CAT.

out. Symptomatic relief is observed immediately. The sputum becomes free of tubercular bacillus in 1–2 weeks and the cavity closes in 8–12 weeks. In some cases, like when the cavity is large and thick walled and there is more than one cavity, second sitting is required after 7–10 days. Of the 120 cases done at CHRC so far, symptomatic relief was seen in 90% of the cases, sputum conversion in 75% cases and radiological improvement in 60% of the cases[14]. Considering the fact that 80% of the patients in this study were chronic cases for whom the secondary line of treatment is very expensive and often constrained because the patient may be resistant to these drugs, the results are significant. Studies on a smaller number of patients have also been carried out at M.Y. Hospital[15], Indore using N_2 laser system built at CAT and L.R.S. Institute of Tuberculosis and Allied Diseases[16], New Delhi using a Russian N_2 laser system. These have also generated promising results providing support for the potential of the technique. The mechanism of therapy is however not well understood. Therefore, more careful clinical studies and investigations on the effect of UV A radiation on immune system and *Mycobacterium tuberculosis* are clearly needed. Some studies on the latter aspect have already been initiated at CHRC and are discussed later in this article.

N_2 laser is also being used regularly at CHRC for treatment of non-healing wounds, ulcers, and burns with rejected grafts. The increased microcirculation of the blood and the lesser bacterial count in the irradiated wound area[17] are expected to play a major role in the faster healing of the wounds (Figure 5). Laser irradiation-induced changes in the proliferation of the epidermal cells may also be playing a role[18] as will be discussed later.

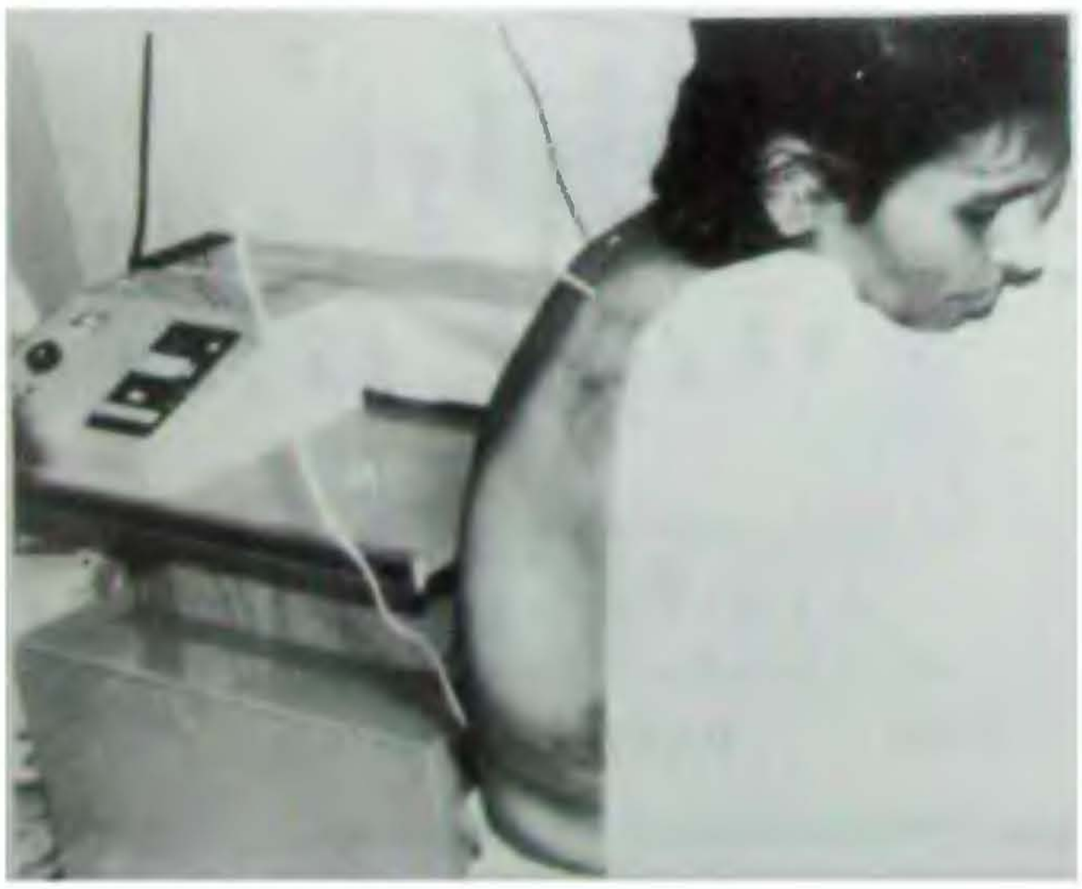

Figure 4. Treatment of pulmonary tuberculosis by irradiating the tubercular cavity by N_2 laser radiation coupled to an optical fibre.

Other laser systems

CAT also has well developed technology for several other lasers used for medical applications, like CW and pulsed Nd : YAG lasers, metal vapour lasers, etc. Development of semiconductor diode lasers (SDLs) and SDL pumped solid state lasers which offer important advantages of compactness and reliable and rugged operation has also been taken up. An all solid state laser system with green output of up to 300 mW has been developed and could prove to be very useful for various medical applications. A 10 W hand held CO_2 laser unit for dermatological applications has also been developed.

Diagnostic applications of lasers

Recently, there has been considerable interest in the use of laser spectroscopic techniques for medical diagnosis. This is motivated by the fact that the onset and the progression of a disease is often accompanied by biochemical/morphological changes which can be sensitively monitored by laser spectroscopic techniques. It

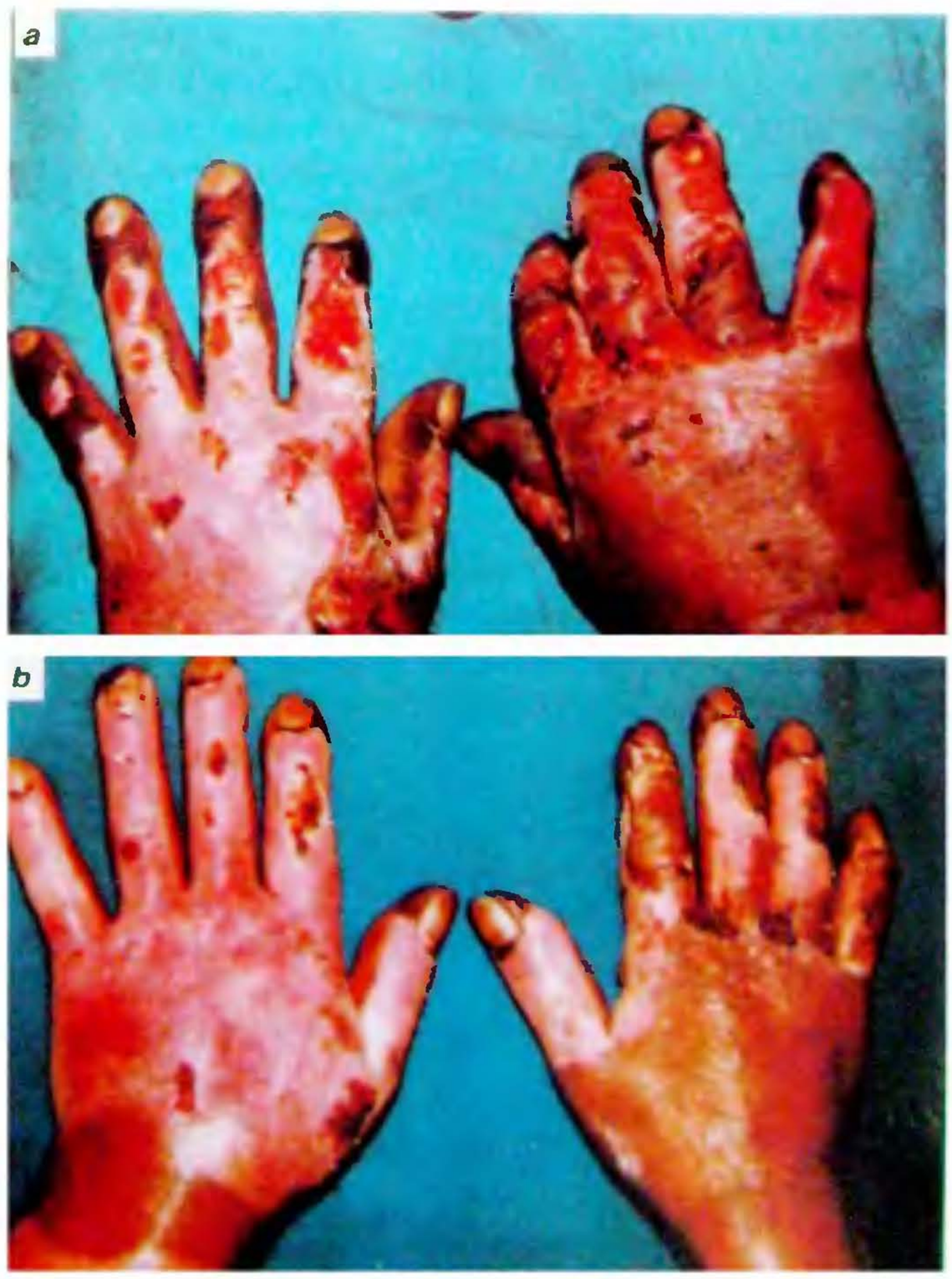

Figure 5. N_2 laser treatment of burn wounds. ***a***, Burn wound infected with *pseudomonas* resistant to all drugs; ***b***, Wound treated with N_2 laser irradiation.

can therefore lead to disease diagnosis at an early stage before the disease becomes difficult to manage. The other important advantages offered by these techniques are their potential for *in situ*, near real time diagnosis and the use of non-ionizing radiation which makes them particularly suited for mass screening and repeated use without any adverse effects. One area where very promising results have already been obtained, and where some work has also been carried out at CAT, is use of laser-induced fluorescence (LIF) from native human tissue for cancer diagnosis.

A schematic of the experimental arrangement being used at CAT for *in vitro* studies on autofluorescence spectroscopy of human tissues is shown in Figure 6. It uses a home-built pulsed N_2 laser, the output of which is coupled to an optical fiber (core diameter 400 μm) via dichroic mirror that reflects N_2 laser radiation (337 nm) and transmits longer wavelength fluorescence output. The power of the laser pulse is monitored by a beam splitter–photodiode combination. The fluorescence from the tissue, kept in contact with the fiber, is collected by the same fiber and imaged on the entrance slit of a scanning monochromator. The wavelength dispersed light at the exit slit of the monochromator is detected by a photomultiplier tube detector. A microprocessor-based system developed at CAT is being used for on-line acquisition of N_2 laser power and fluorescence spectral data. For excitation/emission spectroscopic studies at other wavelengths a commercial spectrofluorometer (SPEX, Fluorolog II) was used. In the following, we briefly summarize the results of the studies carried out at CAT on autofluorescence from tissues from different organs.

Cancer of oral cavity

Oral cancer is one of the most common cancers in India and several other South Asian countries. Laser-induced fluorescence technique is particularly well suited for early detection of oral cancers due to the easy accessibility of this organ. The 337 nm excited autofluorescence spectra from oral tissues (alveolus, buccal mucosa and the tongue tissue samples obtained from patients with the cancer of oral cavity) were characterized, in general, by two major wavelength bands centered around 390 nm and 430 nm and a shoulder around 520 nm (ref. 19). Significant differences were observed in the spectrally integrated fluorescence intensity ($\sum_\lambda I_F(\lambda)$; $360 \le \lambda \le 600$ nm) from cancerous and normal oral tissue sites. In Figure 7 we show the scatter plot for the spectrally integrated intensity for paired cancerous and adjoining normal tissue sites of 12 patients (4 alveolus, 4 buccal mucosa and 4 tongue) selected at random from the patients investigated. The considerably higher values of $\sum_\lambda I_F(\lambda)$ for normal tissue sites is apparent. The mean value of $\sum_\lambda I_F(\lambda)$ from normal tissue sites was larger by a factor of 2 compared to that from cancerous tissue sites. At the other excitation wavelengths (λ_{ex} = 300 nm and 460 nm), no significant difference in fluorescence yield between cancerous and normal oral tissue sites was observed. With 337 nm excitation use of $\sum_\lambda I_F(\lambda)$ alone as a discrimination parameter provided excellent discrimination between cancerous and normal oral tissues. The scatter plots for the values $\sum_\lambda I_F(\lambda)$ from the cancerous and the normal tissue sites of alveolus, buccal mucosa and tongue separately as well as over the total sample size are shown in Figure 8. The sensitivity and specificity values for discriminating cancerous from normal oral tissues were ~90% over the sample size investigated[19]. Use of a stepwise multi-variate linear regression (MVLR) analysis with ten input parameters led to only a marginal improvement in the discrimination results[20]. It is pertinent to note that having a discri-

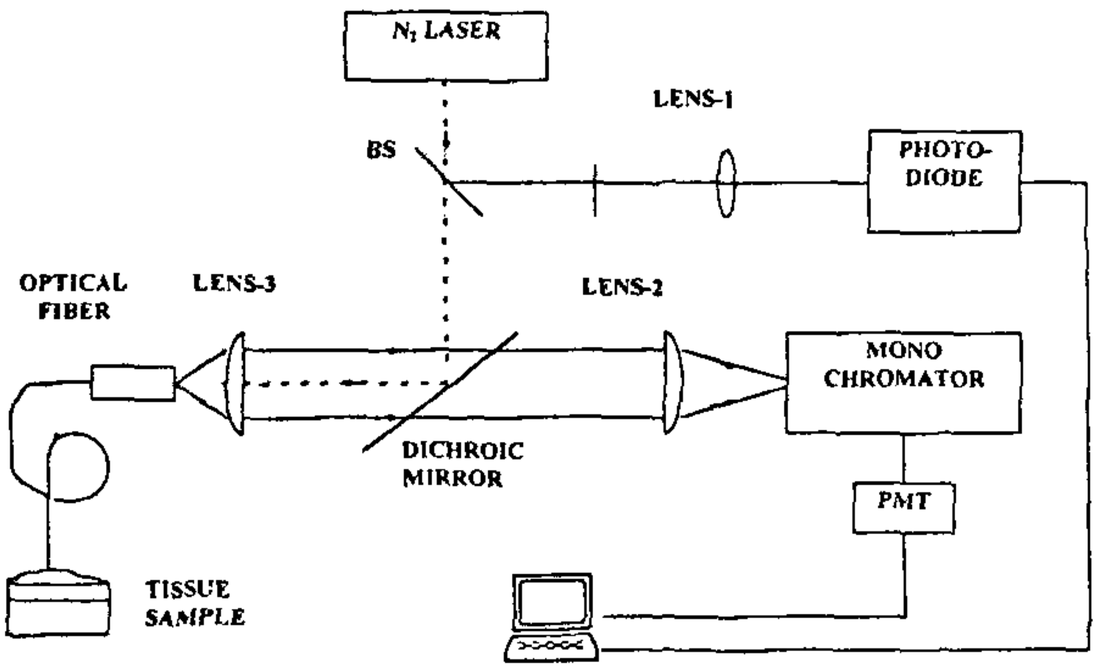

Figure 6. Schematic diagram of the experimental set-up for autofluorescence spectroscopy of tissues.

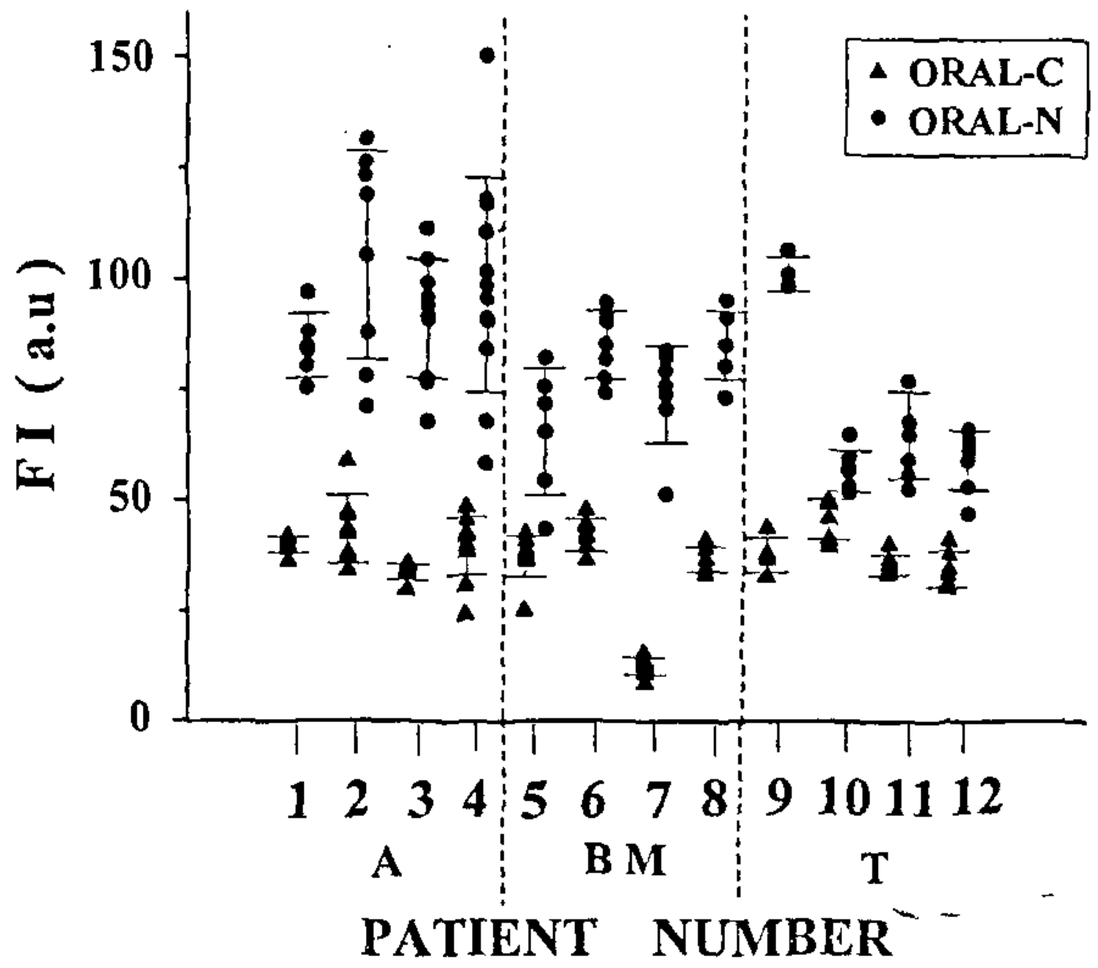

Figure 7. Scatter plot for the integrated fluorescence intensity for N_2 laser excited spectra of paired cancerous and normal oral tissue sites from 12 patients selected at random. Patient nos 1 to 4 had cancer of alveolus (A), 5 to 8 had cancer of buccal mucosa (BM), and 9 to 12 had cancer of tongue (T).

mination parameter based only on $\sum_\lambda I_F(\lambda)$ has the advantage of a much simpler experimental arrangement, since no spectral resolution is required. It can, however, be used as a good discrimination parameter only when the difference in intensity values for malignant and normal sites is much more than the variations possible due to various experimental factors. Applicability to *in vivo* studies therefore needs to be investigated. The LIF-based approach is expected to lead to an early diagnosis and may allow detection of premalignant alterations for which presently no effective non-invasive method exists.

Breast cancer

Autofluorescence spectroscopy of breast tissue with N_2 laser excitation showed that the cancerous tissue was considerably more fluorescent compared to the normal and the benign tumour tissue[21]. A scatter plot for the integrated fluorescence intensity of paired cancerous and adjoining normal breast tissue samples from 10 patients is shown in Figure 9. The ratio of the mean fluorescence intensity for cancerous sites to that from normal and benign tumour sites was ~ 2.82 and 3.23 respectively in this study involving 63 patients; 28 with ductal carcinoma and 35 with fibroadenoma[21]. With 300 nm and 488 nm excitation, the cancerous sites were more fluorescent than the normal. However, no statistically significant difference was observed in the fluorescence intensity of cancerous and benign tumour sites. Therefore, while cancerous tissue could be discriminated from normal with good sensitivity and specificity, the discrimination results were poor for discriminating cancerous from benign tumour tissue. With 337 nm excitation, the use of fluorescence intensity as a discrimination parameter could however, discriminate cancerous tissue from both normal and benign tumour tissue, with sensitivity and specificity values of > 99%.

The reasons for the much better discrimination results obtained with 337 nm excitation, compared with the other excitation wavelengths used by other researchers[22], have also been identified by carrying out excitation/emission spectroscopy at different wavelengths[23] and time resolved measurements[24] on breast tissue autofluorescence.

Although the breast cancer is not a superficial disease, the LIF-based diagnosis can be conveniently done during needle biopsy and can prove a good screening method. This is of interest because X-ray mammography, the best available means of detecting breast cancer at present, has two important drawbacks. First, it leads to a very large number of false positives, i.e. a very large proportion (60–90%) of mammographically abnormal detection turn out to be benign upon invasive breast biopsy[25], leading to avoidable trauma and psychological stress to patients. Secondly, frequent exposure to ionizing X-ray radiation during mammography has potential hazards, howsoever remote. Laser screening can be used without the adverse effects associated with the use of ionizing radiation. Further, the results of the *in vitro* studies suggest that the LIF technique may offer much improved specificity.

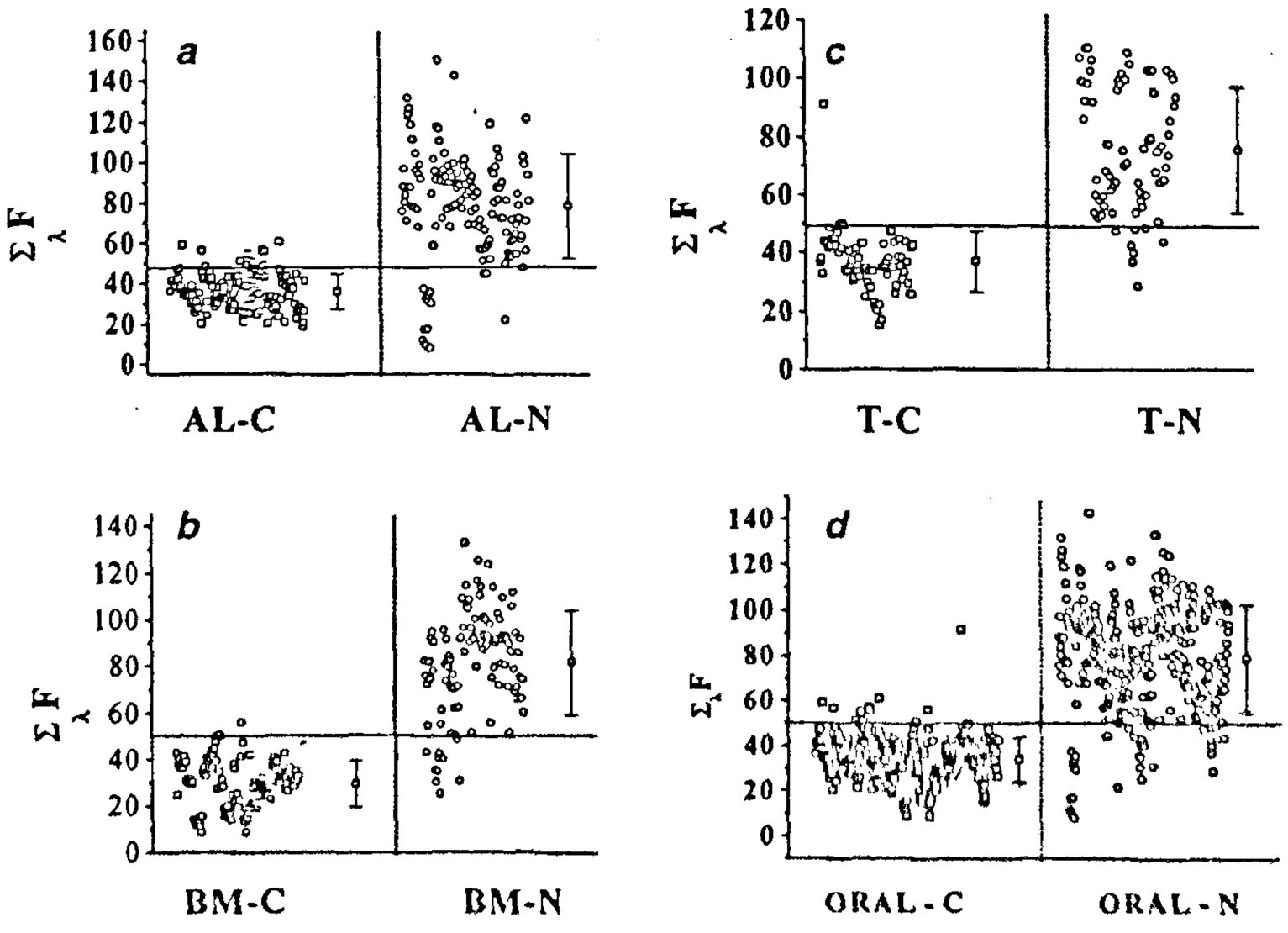

Figure 8. Scatter plot for the spectrally integrated fluorescence intensities from different sites of oral cavity ***a***, alveolus; cancerous (AL-C) and normal (AL-N); ***b***, buccal mucosa; cancerous (BM-C) and normal (BM-N); ***c***, tongue; cancerous (T-C) and normal (T-N); ***d***, from cancerous (ORAL-C) and normal (ORAL-N) sites of the oral cavity over the total sample size investigated. The bars show mean value ± standard deviation.

Uterine cancer

The N_2 laser excited autofluorescence spectra from uterine tissue also showed significant differences between normal and cancerous tissue. The differences in the spectra were quantified using a stepwise MVLR analysis. The discrimination score based on a 4 variable MVLR analysis could discriminate cancerous sites from normal with sensitivity and specificity values of greater than 85% in general and up to 100% when the cancerous site showed red fluorescence characteristic of endogenous porphyrins[26].

Reasons for the spectral differences

An understanding of the factors responsible for the significant differences between the autofluorescence spectra of cancerous, benign tumour and normal tissue sites is clearly very important. This may not only help in optimization of the diagnostic system but may also provide valuable biochemical information on the tissue. Comprehension of the spectral differences requires that the fluorophores present in the different tissue types are identified and their relative concentrations estimated.

The prominent fluorophores in human tissue are believed to be the amino acids, the structural proteins (collagen and elastin), the co-enzyme NADH and the flavins[5]. The absorption and emission maxima (λ_{ex}, λ_{em}) of these are (280 nm, 340 nm), (335 nm, 390 nm), (340 nm, 460 nm), and (430 nm, 520 nm) respectively. This observation is supported by the fact that the excitation spectra recorded from the tissue samples for 340 nm, 390 nm, 460 nm and 520 nm emission consists of spectral bands with peaks around wavelengths which are characteristic excitation peaks for tryptophan, collagen, NADH, and flavin respectively.

The observed fluorescence spectrum is a superposition of the spectra of these fluorophores present in the tissue. However, it is also influenced by the tissue absorption and scattering at both the excitation light and the fluorescence emission. Therefore, quantitative estimation of the concentration of fluorophores from the observed spectra is a formidable task, requiring a detailed knowledge of the tissue optical parameters and a modelling of light propagation in tissues at both the excitation and emission wavelengths[27]. Some information on the relative concentration of the fluorophores can nevertheless be obtained from an analysis of the excitation and emission spectra of tissues. This follows, because a change in the excitation wavelength will lead to a change in the efficiency with which different fluorophores are excited. Similarly, the excitation spectra corresponding to the emission peaks of the fluorophores can provide some idea of the relative concentration of the respective fluorophores. Another approach whereby the same information can be obtained in a single step is to record the synchronous luminescence (SL) spectra from tissues. In this technique[28], the fluorescence signal is recorded by simultaneously scanning both the excitation and emission wavelengths at the same speed with a fixed wavelength interval ($\Delta\lambda$) between the excitation and emission wavelength. Since the technique takes advantages of the absorption as well as the emission properties of a given compound, it leads to considerable simplification in the measured fluorescence spectral profile and reveals a more resolved structure from a composite system (like tissue), in contrast to the generally featureless and broad band appearance of the conventional fluorescence spectra.

The results of excitation/emission[19,23], synchronous luminescences[29] and time resolved studies[24] carried out at CAT on breast and oral cavity tissues suggest a significant variation in the concentration of the fluorophores in the different tissue types. In particular, the studies reveal that while concentration of NADH is higher in malignant breast tissues compared to benign tumour and normal breast tissues[23], the reverse is true for tissues from oral cavity where NADH concentration is higher in normal oral tissues[19]. These results have also been confirmed by enzymatic measurements of NADH concentration in malignant and normal tissues from breast and oral cavity[30]. The differences in fluorophore concentration inferred from spectroscopic studies qualitatively explain the observed spectral differences in the autofluorescence spectra of the oral and breast tissues.

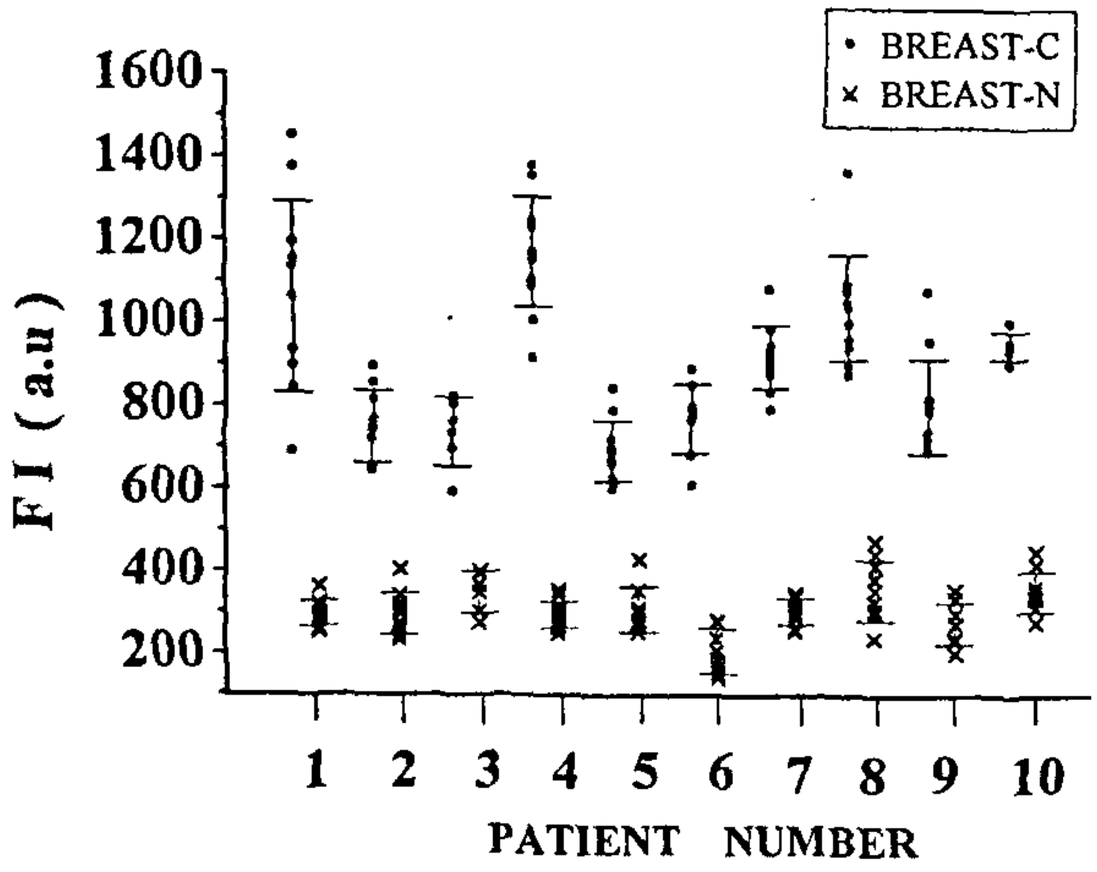

Figure 9. Scatter plot for the spectrally integrated fluorescence intensity of paired cancerous and adjoining normal breast tissue samples from ten patients.

In vivo studies

A schematic of the LIF-based system developed at CAT for *in vivo* clinical studies is shown in Figure 10. It consists of

a sealed-off N_2 laser (7 ns, 100 μJ, 10 Hz), an optical fiber probe, and a gateable intensified CCD detector. The diagnostic probe, developed in-house, is a flexible fiber bundle which has two legs; one contains a single quartz fiber (NA 0.22, core diameter 400 μm) and the other contains six quartz fibers (NA 0.22, core diameter 400 μm). The central fiber delivers excitation light to the tissue surface and the six surrounding fibers collect tissue fluorescence from the surface area directly illuminated by the excitation light. The light coming from the distal ends of the six collection fibers is imaged at the entrance slit of a polychromator coupled to the intensified CCD. The fiber bundle is enclosed in an SS tube (9 mm outer diameter). The tip of the probe is shielded by a quartz optical flat 2 mm thick to provide a fixed distance between the tissue and the fibers for improved fluorescence collection and to protect contamination of the fiber tips with body fluids.

The system has recently been installed at a cancer screening center at Indore for clinical *in vivo* studies on cervical and oral cancer. Both these cancers are widely prevalent in our country and are also easily amenable to LIF technique. In these studies, a qualified doctor will locate the suspected region using the conventional means. However, before the tissue is removed for histopathological assessment fluorescence spectra will be recorded from the suspected site as well as several other surrounding sites. The data-base so created will be analysed to develop discrimination algorithms. These studies will have to be carried out on a large number of patients (few hundred). Further, depending on the discrimination results obtained with the use of N_2 laser excitation, the use of other excitation wavelengths or combination of excitation wavelengths obtained by using a N_2 laser pumped dye laser may also have to be evaluated in order to obtain desired diagnostic efficacy.

Studies on photobioactivation

The use of light for non-surgical therapeutic applications[31] exploits photochemical reactions initiated by photo-excitation of natural chromophores or exogenous drugs localized in the tissue. Some well-known examples of the therapeutic use of light are its use in the treatment of psoriasis, neonatal jaundice, skin tuberculosis, photodynamic therapy of cancer, etc. Several researchers have also reported that irradiation with narrow bandwidth light (laser) can have profound effect on cellular cultures and animal models[32] and can also lead to therapeutic effects in humans[3,4], like accelerated wound healing, relief in pain of different origin, etc. The clinical studies carried out at CHRC have shown the potential of N_2 laser irradiation for treatment of pulmonary tuberculosis, and faster healing of non-healing wounds[11,17]. In addition, He–Ne and SDLs have been used with rather intriguing efficacy for the treatment of pain of various etiologies[33]. It is pertinent to note that for these photo-therapeutic applications any conventional light source generating the appropriate wavelength and with the desired parameters (energy, pulse duration, etc.) can be used. However, the better control on laser light characteristics often makes photo-therapy more convenient with the use of lasers. The mechanisms for many of the photo-therapeutic effects are not very well understood. The clinical potential of this rather simple and inexpensive therapeutic modality is motivating considerable work in this direction and substantial progress is being made[34]. Some studies in this direction are also being carried out at CHRC and CAT.

The *in vitro* studies carried out at CHRC[35] on lawns of microbes on solid nutrient media have shown that N_2 laser radiation has broad antimicrobial effect on micro-organisms ranging from gram-positive organisms like *Staphylococcus aureus* to a variety of gram-negative bacteria, including the multiple drug-resistant *Pseudomonas* and *Klebsiella*. Its antimicrobial effect was also seen on therapy-resistant organisms like *C. albicans* and *Mycobacteria*. The effect of N_2 laser on the phagocytosis of polymorphonuclear leukocytes (PMNL) has also been investigated[36] because the phagocytic activity of these cells is an important defence mechanism against the invading microorganisms. PMNL exposed to nitrogen laser showed increased intracellular killing of the challenged bacteria as against the non-irradiated control PMNL. In diseases like diabetes, the PMNL population of the patient becomes less active and, as a result, are not able to protect against the invading micro-organisms. It is therefore very interesting to note that PMNL even from diabetic patients showed accentuated killing of the challenge bacteria when exposed to N_2 laser[16]. These observations throw some light on the possible mechanisms underlying the improved healing of diabetic ulcers and other non-healing wounds. Studies carried out at CAT[18] showed that N_2 laser irradiation at certain doses can lead to a proliferation of cells in the active epidermal layer of the rabbit/mice skin. Such proliferation of cells can also contribute to faster healing of the wounds. Further, the fact that an inhibition of cell proliferation was

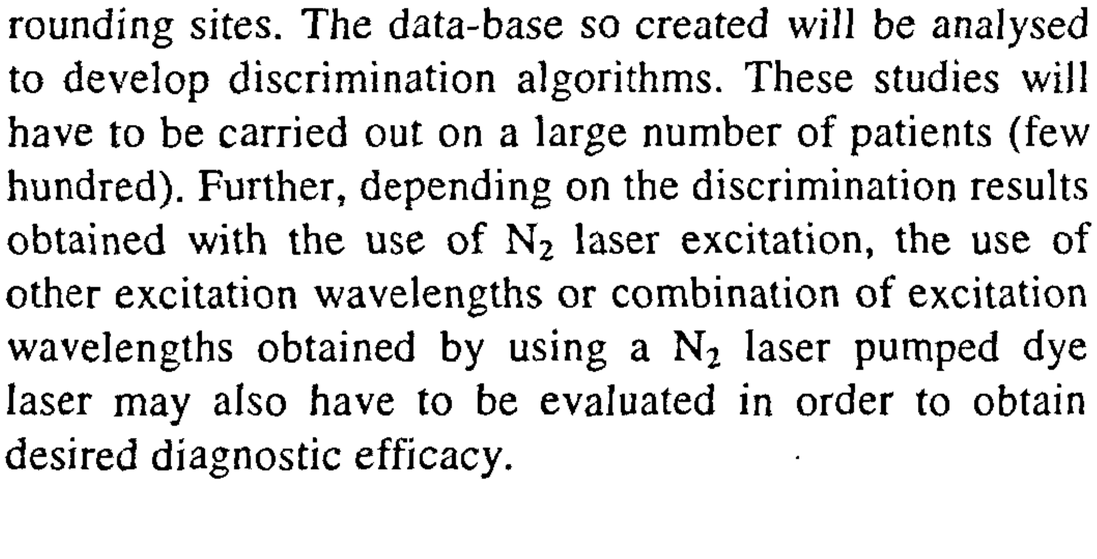

Figure 10. A schematic of the prototype LIF-based system developed at CAT for *in vivo* studies on cancer diagnosis.

observed at higher dose highlights the importance of a careful study of the parametric dependence in order to elicit the desired clinical response.

Macrophages play an important role in the pathology and immunology of tuberculosis as well as wound healing. Therefore, the effect of laser irradiation on macrophages has also been studied at CHRC and CAT. The studies done at both the places show stimulation of macrophage following He–Ne laser irradiation[37–39]. UV-induced DNA damage to macrophages has also been studied using a single cell electrophoresis set up[40].

Studies on narrow bandwidth light effects on *E. coli* bacterial systems carried out at CAT have provided two interesting results. First, it has been observed[41] that He–Ne laser irradiation can stimulate respiratory electron transfer process through change in redox state of respiratory components. Since the production of ATP, the source of cellular energy, is linked to electron transfer such stimulation can lead to enhanced metabolism. Experiments carried out using different inhibitors for the respiratory chain components suggest that the primary photoreceptor at He–Ne laser wavelength is cytochrome d. Secondly, it has been observed[42] that He–Ne laser (632.8 nm) pre-irradiation induces protection towards UVC irradiation in several *E. coli* strains. The magnitude of protection was found to depend on He–Ne laser intensity, exposure time and the period of incubation between He–Ne laser exposure and subsequent UVC irradiation. The results also suggest involvement of singlet oxygen in the He–Ne laser-induced protection.

Some studies on photodynamic effects on cellular cultures and a pilot study on photodynamic therapy of animal tumours have also been initiated at CAT. The latter study is a collaborative work with a group at Radiation Medicine Centre (RMC) to characterize a photosensitiser drug patented jointly by RMC, Mumbai, and IIT, Mumbai.

Conclusions

The use of lasers in various surgical procedures is well established and is expanding rapidly. The surgical CO_2 laser and the N_2 laser systems developed at CAT are being used extensively at CHRC, Indore and other hospitals in the country for a variety of applications.

There also exists considerable current interest in development of laser-based techniques for *in situ*, near real time diagnosis. *In vitro* studies have been carried out at CAT on laser-induced fluorecence of tissues resected at surgery or biopsy from patients suffering from cancer of oral cavity, breast or uterus. These studies have provided very encouraging results for discriminating cancerous tissue sites from benign tumour tissue or normal tissue sites. Encouraged by these, *in vivo* studies on the diagnosis of oral/cervical cancer have been initiated using a prototype LIF-based system developed at CAT.

Photobioactivation using endogenous and exogenous chromophores also holds considerable promise for a variety of therapeutic applications. However, realization of this potential requires developments on two fronts; careful studies on the effects of narrow bandwidth light on cellular cultures and animal models so that the mechanisms responsible for the various photo-therapeutic effects are better understood and development of appropriate photo-therapeutic systems. Activities in both these directions are being carried out at CAT.

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