RC25156 (W1105-016) May 5, 2011
Other

IBM Research Report

Excimer Laser Debridement of Necrotic Erosions of Skin without Collateral Damage

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ABSTRACT

Pulsed ArF excimer laser radiation at 6.4 eV, at fluence exceeding the ablation threshold, will debride burn eschar and other dry necrotic erosions of the skin. Debridement will cease when sufficiently moist viable tissue is exposed, due to absorption by aqueous chloride ions (Cl^-) through the non-thermal process of electron photodetachment, thereby inhibiting collateral damage to the viable tissue.

ArF excimer laser radiation debrides/ablates ~1 micron of tissue with each pulse. While this provides great precision in controlling the depth of debridement, the process is relatively time-consuming. In contrast, XeCl excimer laser radiation debrides ~8 microns of tissue with each pulse. However the 4.0 eV photon energy of the XeCl excimer laser is insufficient to photodetach an electron from a Cl^- ion, so blood or saline will not inhibit debridement. Consequently, a practical laser debridement system should incorporate both lasers, used in sequence. First, the XeCl excimer laser would be used for accelerated debridement. When the necrotic tissue is thinned to a predetermined thickness, the ArF excimer laser would be used for very precise and well-controlled debridement, removing ultra-thin layers of material with each pulse. Clearly, the use of the ArF laser is very desirable when debriding very close to the interface between necrotic tissue and viable tissue, where the overall speed of debridement need not be so rapid and collateral damage to viable tissue is undesirable. Such tissue will be sterile and ready for further treatment, such as a wound dressing and/or a skin graft.

Keywords: laser, burn eschar, debridement, smart scalpel, damage-free, excimer, ArF, XeCl

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1. INTRODUCTION

Surgical debridement is a treatment indicated in the management of deep second and third degree burn injuries, as well as decubitus, stasis and neuropathic ulcers. Necrotic tissue hampers wound recovery and leaves the surrounding healthy tissue vulnerable to infection. Removal of the necrotic tissue through debridement facilitates and encourages a healthy wound healing response. Currently, debridement of necrotic tissue is performed surgically through the use of a scalpel or dermatome. Though experienced hands reduce the risk of the accidental removal of healthy tissue or incomplete removal of the necrotic tissue, the mechanical nature of the treatment inevitably lends itself to some undesirable damage to the wound, resulting in delayed or impaired wound healing and the risk of infection. This shortcoming is amplified in the treatment of wounds located in areas of aesthetic and/or functional significance, such as the face or hands, where minimization of scarring is of the utmost importance. Complete dermal preservation, therefore, is critical for re-epithelialization. Successful debridement can thus optimize natural wound healing or, in more extensive injuries, provide a platform conducive to skin grafts. This technique can also aid in the treatment of chronic wounds, promoting wound healing by providing controlled and precise removal of necrotic tissue from the wound region, while leaving healthy underlying and adjacent tissue intact.

We propose a practical debridement system employing two lasers, a 308 nm (4.0 eV) XeCl excimer laser, serving as the "coarse sandpaper" to rapidly debride the bulk of the necrotic areas to the point where the remaining necrosis is sufficiently thinned, at which point the system will switch to the shorter wavelength 193 nm (6.4 eV) far ultraviolet ArF excimer laser that will act as the "ultra fine sandpaper," debriding the remaining necrotic areas and ceasing debridement when viable tissue is exposed.

Irradiation in the vacuum ultraviolet (i.e., ultraviolet light at wavelengths shorter than 200 nm, which is absorbed by the oxygen in air) with photons of 6.4 eV energy, derived from an ArF excimer laser, has the potential to be the "smart scalpel" that will debride relatively dry necrotic tissue, e.g. burn eschar, yet produce no significant temperature rise or collateral damage to the adjacent and underlying viable tissue, because of the way light interacts with electronic states of atoms and ions. Thus, the ArF excimer laser is an excellent candidate to replace "cold steel" for debridement, offering the promise of a paradigm shift in the way necrotic lesions of skin are treated.

2. BACKGROUND AND CONCEPT

There have been many studies on the use of alternative techniques to debride necrotic tissue, including the use of chemical techniques and various laser techniques.

In 1981, Blum *et al* [1] found that tissue strongly absorbs the short pulses of 6.4 eV radiation from an ArF excimer laser. At irradiation fluence above the ablation threshold, sufficient light energy is absorbed by very thin layers (~0.5 micron thick) of tissue, which turn rapidly into a gas that is expelled from the surface, carrying away essentially all of the deposited light energy in much less time than required for excess heat to diffuse into adjacent tissue. Hence, the residual collateral damage is negligible. When applied to mammalian cornea *in vivo*, the cornea may be reshaped to correct refractive errors (e.g., myopia, astigmatism, hyperopia), and the reshaped cornea heals without clouding or scarring. [2]

In 1983, Lane *et al* [3, 4] irradiated the skin of live guinea pigs with 193 nm (6.4 eV) radiation from an ArF excimer laser, as well as with 248 nm (5.0 eV) radiation from a KrF excimer laser. They discovered that 193 nm laser radiation failed to remove (ablate) tissue after bleeding commenced. In contrast, 248 nm radiation continued to ablate tissue, despite bleeding. 6.4 eV radiation is strongly absorbed by an aqueous salt solution, as found in blood, through the process of electron photodetachment from hydrated chloride ions (Cl^-), with a characteristic resonance absorption maximum at 6.5 eV. Such an electronic excitation does not produce heat. This process depletes the laser fluence sufficiently to suppress further ablation of protein and lipids in tissue and/or blood.

In 1991, Eldad *et al* [5] examined several treatment modalities for partial thickness chemical burns of live guinea pigs: surgical excision; laser ablation, and chemical debridement. They found that ablation with the ArF excimer laser was most effective and accelerated healing of burn lesions after "dry" exposure to 5 mg of nitrogen mustard. The wound-healing score of the laser-treated burns was higher on day 4 compared to untreated controls. Laser ablation enabled control of the amount of tissue to be removed with minimal blood loss. However, at the time this study was carried out,

the laser equipment available made the technique rather time consuming. They concluded that this therapy could not be applied for large burns.

Eldad *et al* [5] did not know about Lane *et al's* [3, 4] results and the fact that aqueous Cl^- was stopping the ArF irradiation from creating collateral damage to the underlying and adjacent viable tissue. In fact, when the paper [5] describing their results was written in 1997 and subsequently published in 1998, the subset of the authors who actually composed the paper did not know which excimer laser had been used. They mistakenly wrote that it was an "Excimer laser (308nm in xenon gas)." In fact, it was a 193nm (6.4 eV) ArF excimer laser. [6]

In 1992, Green *et al* [7] studied skin graft take and healing of full-thickness wounds in live pigs, created with a cold-steel scalpel through the dermis and subcutaneous tissue to the muscle fascia, following by uniform laser ablation of the muscle fascia graft bed using four different types of lasers. The residual thermal damage caused by continuous-wave carbon dioxide and the pulsed Holmium:YAG lasers significantly exceeded 160 microns in depth, because the light energy absorbed in the irradiated tissue was converted into heat which diffused into the adjacent tissue before the surface tissue that was vaporized had time to escape (i.e., to be ablated) from the irradiated surface. Under these circumstances, skin graft take was impeded, due to "delayed graft revascularization, increased inflammatory cell infiltration, and accelerated formation of hypertrophic fibrous tissue formation within the graft bed." In contrast, " …. ArF excimer lasers …. create wound beds with minimal thermal damage, permitting graft take comparable to that achieved with standard surgical techniques."

Neither Eldad *et al* [5] nor Green *et al* [7] recognized the fact that 6.4 eV photons from the ArF laser have sufficient energy to photodetach an electron from an aqueous Cl^-. To our knowledge, there is nothing published in the medical literature, prior to our work, that recognizes the importance of this fact.

In the study by Lane *et al* [3, 4], ArF and KrF excimer lasers were used to irradiate the skin on the backs of live guinea pigs. When ablation of the dermis commenced and blood capillaries were impacted, the 193 nm ArF excimer laser radiation failed to remove tissue. The 248 nm KrF excimer laser radiation, however, continued to remove tissue, despite bleeding. Lane *et al* measured the transmission of ultraviolet light through 1 mm of physiologic saline solution, finding only ~1% transmission at 193 nm (6.4 eV). In contrast, virtually 100% transmission occurred at 248 nm (5.0 eV). They identified "the absorption mechanism at 193 nm as electron charge transfer from hydrated chloride ions (Cl^-) to water, since this mechanism has a characteristic resonance absorption maximum at 190 nm. In this process, the energy of the 6.4 eV photons goes into detaching an electron from Cl^-, changing it into a hydrated electron and leaving a hydrated Cl atom. Since this process has a large absorption cross section for 6.4 eV radiation, insufficient light energy remains to produce thermal ablation of protein or lipids in blood and/or tissue."

The aqueous chloride ions in viable tissue are a strong absorber of ultraviolet radiation at wavelengths below 200 nm (photon energies above 6.2 eV), with an absorption maximum at 190 nm. So the "salt water" that is a major component of viable tissue will "block" the incoming UV light and completely halt the ablation process. The optical absorption spectrum of physiological saline solution shows extremely strong absorption at 193nm. The mechanism of this absorption is the photodetachment of electrons from chloride ions, leaving chlorine atoms and solvated electrons dissolved in the aqueous medium. After each short laser pulse, on a time scale that is very long compared to ablation and thermal diffusion times, the electrons will gradually encounter neutral chlorine atoms and recombine to form chloride ions, giving up the photodetachment energy to heat that will thermally diffuse into the surrounding tissue, resulting in minimal temperature rise of no consequence to the viability or morphology of the underlying tissue.

In summary, the 193 nm (6.4 eV) radiation generated by the ArF laser has sufficient fluence (greater than the ablation threshold fluence) to effectively ablate burn eschar or other necrotic tissue. When all of the eschar or other necrotic tissue in the field of the laser beam has been ablated, the exposed viable tissue, containing Cl^- dissolved in an aqueous environment (e.g., blood, blood plasma, lymph, moist viable tissue), will strongly absorb the 6.4 eV radiation without being ablated or thermally damaged. The absorption mechanism by Cl^- is photodetachment of electrons from hydrated Cl^-. In this process, the 6.4 eV photons strip electrons from the chloride ions, producing hydrated Cl atoms and hydrated electrons. This process severely depletes the laser fluence, and this diminished fluence is insufficient to ablate or otherwise damage the viable tissue.

3. PRACTICAL DEBRIDEMENT SYSTEM

Despite favorable results obtained with ArF excimer laser irradiation, laser debridement has not had significant impact on the standard surgical practice of necrotic skin lesion debridement, presumably because of the relatively low pace of debridement when compared to cold steel methods.

ArF excimer laser radiation is so strongly absorbed by tissue that only ~1 micron of tissue is debrided/ablated with each pulse, provided that the laser fluence exceeds the ablation threshold for that type of tissue. While this provides great precision in controlling the depth of debridement, it results in a relatively time-consuming debridement process. In contrast, longer wavelength (lower photon energy) laser irradiation, e.g., XeCl excimer laser irradiation, at 308 nm (4.0 eV), is less strongly absorbed by tissue, debriding a significantly greater thickness of tissue with each pulse. However the photon energy of these lower photon energy lasers will be insufficient to photodetach an electron from a Cl^- ion, so blood or saline will not inhibit debridement.

This suggests that a practical laser debridement system should incorporate two ablating lasers with different wavelengths that are used in sequence. The first laser, e.g., a 308 nm XeCl excimer laser, would be used for accelerated debridement, removing ~8 microns of tissue with each pulse. When the necrotic tissue is thinned to a predetermined thickness, the second laser, a 193 nm ArF excimer laser, is used for very precise and well-controlled debridement of necrotic tissue, removing ultra thin layers of material with each pulse. Clearly, the use of the ArF laser is very desirable when debriding very close to the interface between necrotic tissue and viable tissue, where the overall speed of debridement need not be so rapid.

The decision to switch from the XeCl laser to the ArF laser may be made by human judgment or by measuring the optical signature (e.g., darkness, color/hue, surface roughness) of the thinned necrotic tissue. A CCD color camera could be used to provide an image on a monitor and/or feed its signal into a device containing image processing software.

To improve efficiency, a method is needed to automatically detect when eschar has been completely debrided from an area being irradiated, exposing viable tissue, whereupon the debriding laser beam(s) will be shifted to irradiate an adjacent area of eschar. One approach is to employ an additional light source, having a wavelength specifically selected to detect the Cl atoms that are produced when the ArF radiation photodetaches electrons from the Cl^- ions. The specificity arises from the fact the Cl atoms have well-defined electronic transitions that are only excited by specific wavelengths of light. Thus, the presence of Cl atoms can be detected by observing the sudden increase of backscatter from this additional light source or by multi-photon laser-induced fluorescence resulting from two-photon absorption of the additional light source. The detection of Cl atoms will provide a signal to terminate the irradiation of the area of tissue that is now free of burn eschar, by shuttering the debriding ArF laser beam or shifting it to a different location to irradiate an area of unirradiated or incompletely debrided burn eschar. More specifically, well-defined one-photon electronic transitions in chlorine atoms are excited by light at the infrared wavelengths 838nm and 859nm. Suitable sources of light at these wavelengths are well known. In particular, the titanium-sapphire laser may be tuned to either of these two wavelengths, or a thermally tuned diode laser may be tuned to emit light at 838nm or 859nm, exactly resonant with these electronic transitions in chlorine atoms. A well-defined two-photon electronic transition in chlorine atoms is excited by light at the ultraviolet wavelength 233 nm. A suitable source of light at this wavelength is well known. In particular, frequency-quadrupled light (at 233 nm), derived from a titanium-sapphire laser or a thermally tuned diode laser emitting light at 932 nm, will excite two-photon laser-induced fluorescence at a wavelength that is characteristic of chlorine atoms. Such light can easily be detected by known means and spectrally separated from all other sources of light, permitting very sensitive detection of the initial appearance of chlorine atoms. This would be an indicator that moist, viable tissue has been unveiled.

4. EXPERIMENTAL RESULTS

At the time this manuscript was written, we had not carried out any new experiments on live animals, since such experiments are not permitted in IBM facilities. However, we have developed collaborations with external medical institutions. By the time our paper is presented on May 26, 2011, we hope to have new experimental results determining the optimum 193 nm ArF excimer laser fluence for debriding necrotic erosions, *in vivo*, while rendering viable tissue sterile and free of collateral damage. Biopsies and cultures of the irradiated residual tissue should demonstrate such tissue suitable for skin grafting with minimal risk of infection. The success of actual skin grafts should validate the effectiveness of this technique.

While *in vivo* experiments at IBM facilities are forbidden, there is no prohibition of *in vitro* experiments. Therefore, at the IBM Watson Research Center, we carried out an experimental study using a 308 nm XeCl excimer laser (Coherent, Model LPXpro 305), with which we irradiated pig skin, *in vitro*, that had been charred using the flame from a propane torch. This irradiation debrided the burn eschar, leaving the underlying skin relatively free from damage.

Figure 1 is a digital photograph of a region of pigskin, obtained from slaughter, from which three samples, each measuring several cm^2 in area, were excised. These samples consisted of full thickness skin (epidermis plus dermis) plus some underlying, attached fat.

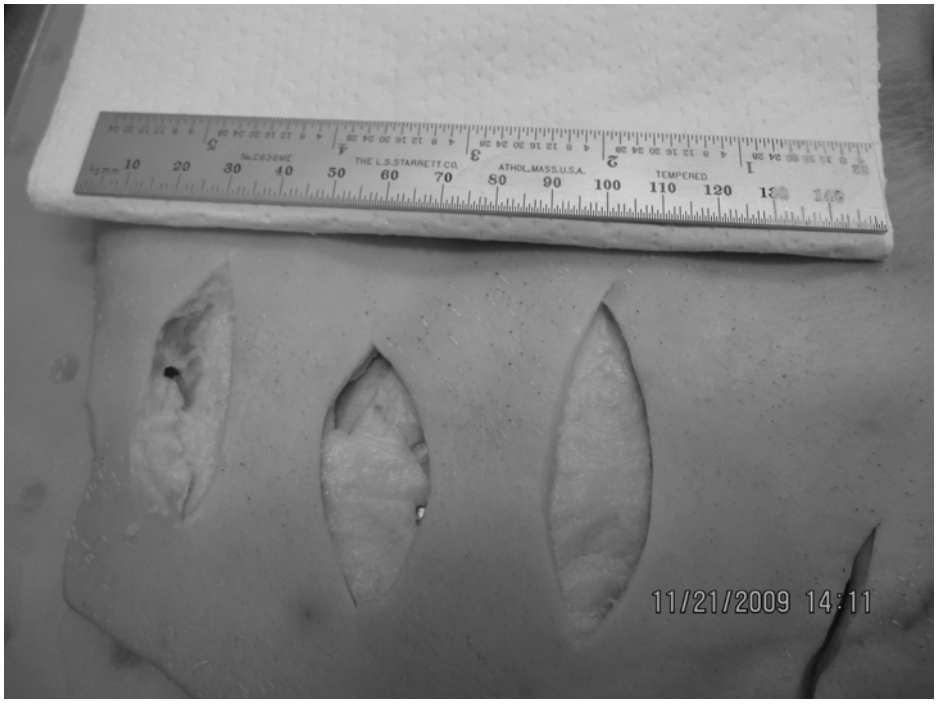

Figure 1. Pig skin, acquired from slaughter, showing three regions where samples, consisting of full thickness epidermis/dermis layers plus underlying fat, were excised

Figure 2 is a digital photo of one of these samples that has been charred by application of a flame from a propane torch.

Figure 2. Pig skin sample, measuring ~2 cm^2 in area, after exposure to the flame of a propane torch. The burn eschar is clearly seen on the surface of the skin.

The XeCl laser delivered ~20 ns long pulses at a rate of 50 Hz, each pulse having an energy of ~0.6 J and a beam cross sectional area of ~0.25 cm^2, for a fluence of ~2.4 J/cm^2 /pulse. The laser beam was scanned over a ~2 cm^2 area of charred skin for ~55 sec, utilizing ~30% of the beam cross section, so a total of ~2750 pulses of light delivered ~500 J of energy with a total fluence of ~250 J/cm^2. Figure 3 is a digital photo of the same previously-charred sample shown in Figure 2, but after 308 nm XeCl excimer laser irradiation, showing complete debridement of the burn eschar, with the exception of multiple small regions where the initial eschar thickness was greater that that covering most of the skin sample.

Figure 3. The same skin sample shown in Fig. 2, but after debriding the burn eschar by irradiation with the XeCl laser.

In this experiment, we did not measure the thickness of the burn eschar produced by the propane torch flame, so we do not have a quantitative measure of the debridement rate from this experiment. However, Nakajima *et al* [8] report a debridement rate of ~8 microns/pulse for burn eschar produced on live rabbits, using XeCl excimer laser with a fluence of 2.5 J/cm^2, comparable to the fluence we used. Their data validates our concept of using a longer wavelength (lower photon energy) laser, such as the XeCl excimer laser, as the "coarse sandpaper" debridement tool for accelerated debridement in the first step of a two-laser debridement process.

5. CONCLUSIONS

In 1997, Wynne and Felsenstein [9] conceived using the precision of tissue removal by the ArF excimer laser to create a tool that followed the contours of the boundary between epidermis and dermis, thereby ablating epidermis while leaving the underlying dermis intact with no collateral damage. This concept was based on the fact that epidermis contains melanin, whereas dermis lacks melanin (except for that located in hair follicles). Experiments on pig skin, *in vitro*, were undertaken at the IBM Watson Research Center in 2001 – 2002, demonstrating that the detection of a color change, as the melanin-containing epidermis was thinned, provided an indication of when the epidermal/dermal interface had been reached. These unpublished results, combined with Lane *et al*'s [3,4] published results from experiments undertaken in 1983, laid the groundwork for the present realization that the ArF excimer laser can be a revolutionary tool for debridement of necrotic tissue.

We note that when Lane *et al*'*s* [4] paper was published in Archives of Dermatology in 1985, John A. Parrish, M.D., founder of the Wellman Center for Photomedicine at Massachusetts General Hospital in Boston, wrote an editorial [10] in which he stated "Results of preliminary studies have suggested that precision tissue ablation with ultraviolet (UV) lasers has the potential for clinical application in corneal surgery. In this issue of the ARCHIVES, Lane *et al* show that skin can also be cut by pulsed UV lasers. Potential applications in skin might include (1) manipulation of the barrier function by precise removal of portions of the stratus corneum; (2) controlled removal of epidermal lesions, especially if recognizable borders give the therapist indications of margins; (3) eschar removal in burn therapy; and (4) precision surgery."

The ArF excimer laser clearly has the potential to be the tool that replaces "cold steel" for debridement, offering the promise of a paradigm shift in the way necrotic lesions of skin are treated. Irradiation in the vacuum ultraviolet (i.e., ultraviolet light at wavelengths shorter than 200 nm, which is absorbed by the oxygen in air) with photons of 6.4 eV energy, derived from an ArF excimer laser, may be the "smart scalpel" that will debride relatively dry necrotic tissue, e.g., burn eschar, yet produce no significant temperature rise or collateral damage to adjacent and underlying viable tissue, because of the way light interacts with electronic states of atoms and ions.

When the necrotic erosions are thick and/or extensive in area, enhanced speed of debridement may be achieved by a two-laser system. The first laser, a longer wavelength (lower photon energy) ultraviolet laser, e.g., a 308 nm (4.0 eV) XeCl excimer laser, will act as "coarse sandpaper" to rapidly debride the bulk of the necrotic areas to the point where the remaining necrosis is sufficiently thinned, at which point the system will switch to the shorter wavelength 193 nm (6.4 eV) far ultraviolet ArF excimer laser that will act as the "ultra fine sandpaper," debriding the remaining necrotic areas and ceasing debridement when viable tissue is exposed. This ultraviolet laser-based smart scalpel will debride necrotic areas of the skin, producing no collateral damage to the underlying and adjacent viable tissue, leaving the tissue free of infectious agents and ready for a healing process that is far less traumatic than that which follows cold steel debridement.

In this age of terrorist attacks and on-going wars, where non-combatant citizens and military personnel are exposed to devastating weaponry, including improvised explosive devices (IEDs), producing thermal injuries and chemical burns, the medical community needs a device capable of rapid, efficient, and meticulous debridement of necrotic tissue of any etiology. Such a device would yield accelerated healing, decreased risk of infection, a favorable environment for skin graft take, reduced scarring, and the elimination of laborious "cold-steel" surgery.

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