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Collateral Damage-Free Debridement Using 193 nm ArF Laser

James J. Wynne[1], Jerome M. Felsenstein[2], Robert Trzcinski[1], Donna Zupanski-Nielsen[1], Daniel P. Connors[1]

[1]IBM Research Division
Thomas J. Watson Research Center
P.O. Box 218
Yorktown Heights, NY 10598

[2]100 South Highland Avenue
Ossining, NY 10562

Research Division
Almaden - Austin - Beijing - Cambridge - Haifa - India - T. J. Watson - Tokyo - Zurich

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James J. Wynne*[a], Jerome M. Felsenstein[b], Robert Trzcinski[a],
Donna Zupanski-Nielsen[a], Daniel P. Connors[a]

[a]IBM T. J. Watson Research Laboratory, P.O. Box 218, Yorktown Hts., NY, USA 10598-0218;
[b]100 South Highland Ave., Ossining, NY 10562

ABSTRACT

Burn eschar and other necrotic areas of the skin and soft tissue are anhydrous compared to the underlying viable tissue. A 193 nm ArF excimer laser, emitting electromagnetic radiation at 6.4 eV at fluence exceeding the ablation threshold, will debride such necrotic areas. Because such radiation is strongly absorbed by aqueous chloride ions through the non-thermal process of electron photodetachment, debridement will cease when hydrated (with chloride ions) viable tissue is exposed, avoiding collateral damage to this tissue. Such tissue will be sterile and ready for further treatment, such as a wound dressing and/or a skin graft.

1. INTRODUCTION

Surgical debridement is a treatment indicated in the management of deep second and third degree burn injuries. Severe burn injuries result in necrotic tissue which 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, since a precise and controlled removal of necrotic tissue from wounds, which leaves healthy underlying and adjacent tissue intact, will promote wound healing.

In 1983, Lane *et al* [1, 2] irradiated the skin of live guinea pigs with 193 nm radiation from an ArF excimer laser, as well as with 248 nm 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. 193 nm radiation (at 6.4 eV) 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 190 nm. 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.

We apply this knowledge to propose a novel technique to debride necrotic tissue associated with burns, decubitus, stasis, and neuropathic ulcers, without causing collateral damage to adjacent and underlying viable tissue. Results will be presented demonstrating that excimer laser irradiation of charred pig skin, *in vitro*, debrides burn eschar, while leaving the underlying skin relatively free from damage.

*jjwynne@us.ibm.com; phone 1 914 945-1575; www.research.ibm.com

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. Unfortunately, all have failed to avoid damage to adjacent viable tissue during debridement of the necrotic tissue. Green *et al* [3] concluded that "ablative lasers developed for cutaneous surgery should create less than 160 (+/- 60) microns of residual thermal damage to permit optimal skin graft take and healing. Pulsed carbon dioxide and ArF excimer lasers may be valuable instruments for the removal of full-thickness skin, skin lesions, and necrotic tissue, since they create wound beds with minimal thermal damage, permitting graft take comparable to that achieved with standard surgical techniques." Green *et al* used four different types of lasers. The residual thermal damage caused by the continuous-wave carbon dioxide laser and the pulsed Holmium:YAG laser significantly exceeded 160 microns, 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."

Blum *et al* [4] 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. [5]

In 1983, Lane *et al* [1, 2] used two different excimer lasers, 193 nm ArF and 248 nm KrF, to irradiate the skin on the backs of live guinea pigs. Initially, relatively dry epidermis was ablated by irradiation with these excimer lasers. However, when ablation of the dermis commenced and blood capillaries were impacted, an unanticipated result was observed. As reported "*In vivo*, the 193 nm laser radiation failed to remove tissue after bleeding began. The 248 nm radiation, however, continued to remove tissue, despite bleeding, and left a clean incision with only minimal thermal damage." To understand the basis of this difference, Lane *et al* measured the transmission of ultraviolet light through 1 mm of physiologic saline solution, finding only ~1% transmission at 193 nm. In contrast, virtually 100% transmission occurred at 248 nm. 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."

In greater detail, viable tissue differs from the burn eschar or other necrotic tissue in a very important way: as described above, the aqueous chloride ions in viable tissue are a strong absorber of ultraviolet radiation at wavelengths below 200 nm, 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.

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. 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.

In summary, the 193 nm (6.4 eV) radiation generated by the ArF laser effectively ablates 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 chloride ions dissolved in an aqueous environment (e.g., blood, blood plasma, lymph, moist viable tissue), will strongly absorb the 193 nm radiation without being ablated or thermally damaged. The absorption mechanism by chloride ions is a consequence of photodetachment of electrons from hydrated chloride ions. Basically, the energy from the 193 nm radiation strips electrons from the chloride ions, producing hydrated chlorine atoms and hydrated electrons. The 193 nm radiation is so depleted by this process that there is insufficient fluence absorbed by the viable tissue to ablate or otherwise damage this viable tissue.

Despite these 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.

3. PRACTICAL DEBRIDEMENT SYSTEM

193 nm ArF excimer laser radiation is so strongly absorbed by tissue that only ~1 micron of tissue is debrided/ablated with each pulse. While this provides great precision in controlling the depth of debridement, it results in a relatively time-consuming debridement process. In contrast, 308 nm XeCl excimer laser irradiation is less strongly absorbed by tissue, debriding ~5 microns of tissue with each pulse. However the 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 two ablating lasers with different wavelengths that are used in sequence. The first laser, a 308 nm XeCl excimer laser, is used for accelerated debridement. 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. Alternative, the switching from XeCl to ArF may be determined automatically by measuring the optical signature (e.g., darkness, color/hue, surface roughness) of the thinned necrotic tissue. For example, 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 applications.

In the case of burn eschar debridement, it is important to minimize the time expended on complete eschar removal, because of the critical status of the burn victim. Therefore, 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 necrotic tissue.

4. EXPERIMENTAL RESULTS

At the time this manuscript was written, we have not carried out any new experiments on live animals, since such experiments are not permitted in IBM facilities. However, we have developed collaborations with medical institutions in Boston, MA, and San Antonio, TX. By the time our paper is presented on Jan. 22, 2011, we expect to have new experimental results determining the optimum 193 nm ArF 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 will

demonstrate such tissue suitable for skin grafting with minimal risk of infection. The success of actual skin grafts will validate the effectiveness of this technique.

The experiments we have undertaken at the IBM Watson Research Center employed a 308 nm XeCl excimer laser, with which we irradiated pig skin, *in vitro*, that had been charred using a propane torch. This irradiation debrided the burn eschar, leaving the underlying skin relatively free from damage.

Figure 1 is a digital photo of a region of pigskin, obtained from slaughter, from which three samples, 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 or ~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.
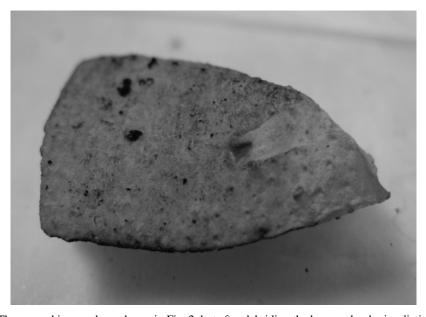

Figure 3. The same skin sample as shown in Fig. 2, but after debriding the burn eschar by irradiation with the XeCl laser.

5. CONCLUSIONS

When Lane *et al*'s[2] 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[6] 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."

In 1997, Wynne and Felsenstein[7] 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. The 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 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 envision a "smart scalpel," enabled by the intrinsic advantage afforded by non-thermal absorption of 6.4 eV ultraviolet light by aqueous chloride ions. When the 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 XeCl excimer laser, will act as "rough 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 far less traumatic than that which follows cold steel debridement.

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