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# Critical Review of Burn Depth Assessment Techniques: Part I. Historical Review

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The assessment of burn depth, and as such, the estimation of whether a burn wound is expected to heal on its own within 21 days, is one of the most important roles of the burn surgeon. A false-positive assessment and the patient faces needless surgery, a false-negative one and the patient faces increased length of stay, risks contracture, and hypertrophic scar formation. Although many clinical signs can aid in this determination, accurate assessment of burn depth is possible only 64 to 76% of the time, even for experienced burn surgeons. Through the years, a variety of tools have become available, all attempting to improve clinical accuracy. Part 1 of this two-part article reviews the literature supporting the different adjuncts to clinical decision making is, providing a historical perspective that serves as a framework for part 2, a critical assessment of laser Doppler imaging. (*J Burn Care Res* 2009;30:937-947)

A burn wound is categorized as first, superficial second, deep second or third degree corresponding to a clinical assessment of depth of thermal injury. Particularly important is the differentiation between superficial and deep second-degree injuries. The reason for this distinction is to try and predict whether the wound will heal by itself within 14 to 21 days or will require excision and grafting for optimal healing. The problem is self-evident. With a false-positive assessment, needless surgery will be performed. With a false negative, the patient faces increased length of stay in the hospital, contracture, and hypertrophic scar formation. The standard way to make this assessment involves the judgment of the clinician evaluating the wound. Aspects such as pain and tenderness, formation of blisters, appearance of the dermis, whether pink, white, grayish yellow, or reddish brown, and whether it blanches or not help guide this decision.<sup>1-4</sup> Addition of a pin-prick test in adults<sup>5</sup> or a modified pin-prick test in children also helps because it involves no extra time to perform, involves no

distress, and helps improve accuracy of assessment.<sup>6</sup> The determination of burn depth and whether a wound will heal spontaneously within 21 days, however, is around 50% for inexperienced surgeons.<sup>7</sup>

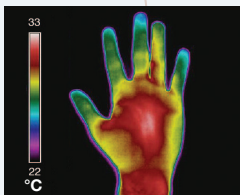
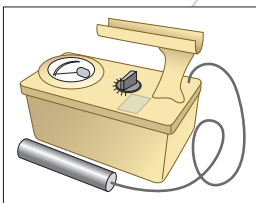
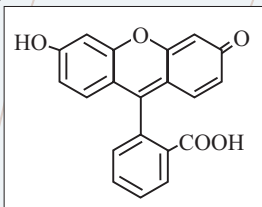
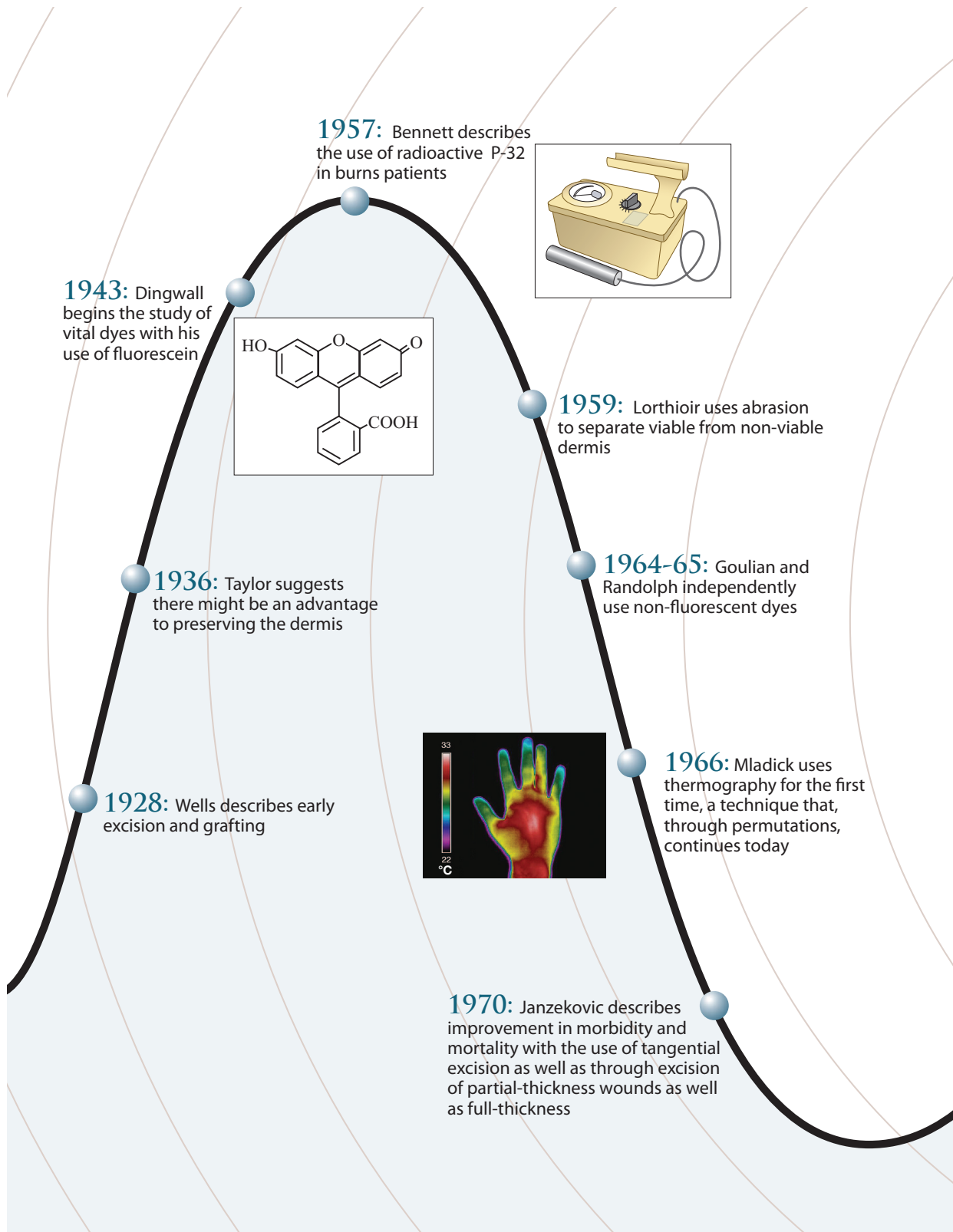
The advent of digital photography brought with it the possibility of telemedicine, where a clinician inexperienced in burn care in a remote location could transmit visual information about the wound to a more experienced surgeon to make the determination of depth. Correlation between compressed and noncompressed digital images and clinical assessment are in the range of 90% for experienced surgeons.<sup>8</sup> Although telemedicine offers a clear advantage in communication between clinicians, particularly with respect to potential transfer of patients from remote areas or in areas with limited resources,<sup>9</sup> the assessment of depth remains a visual one. Although some clinicians have elevated this determination to an art form; even performing serial clinical assessments,<sup>10</sup> the best clinical estimates of burn depth range from 64 to 76% for experienced surgeons.<sup>11,12</sup> As an aide in making the prediction of healing, some have suggested performing serial biopsies looking for the presence of viable dermal tissue and adnexal structures.<sup>13</sup> The numbers are so disappointing that some have suggested that the only time to accurately assess the depth of a burn is during wound excision in the operating room.<sup>2</sup> The need for an early determination is underscored by the fact that there is a shorter hospital

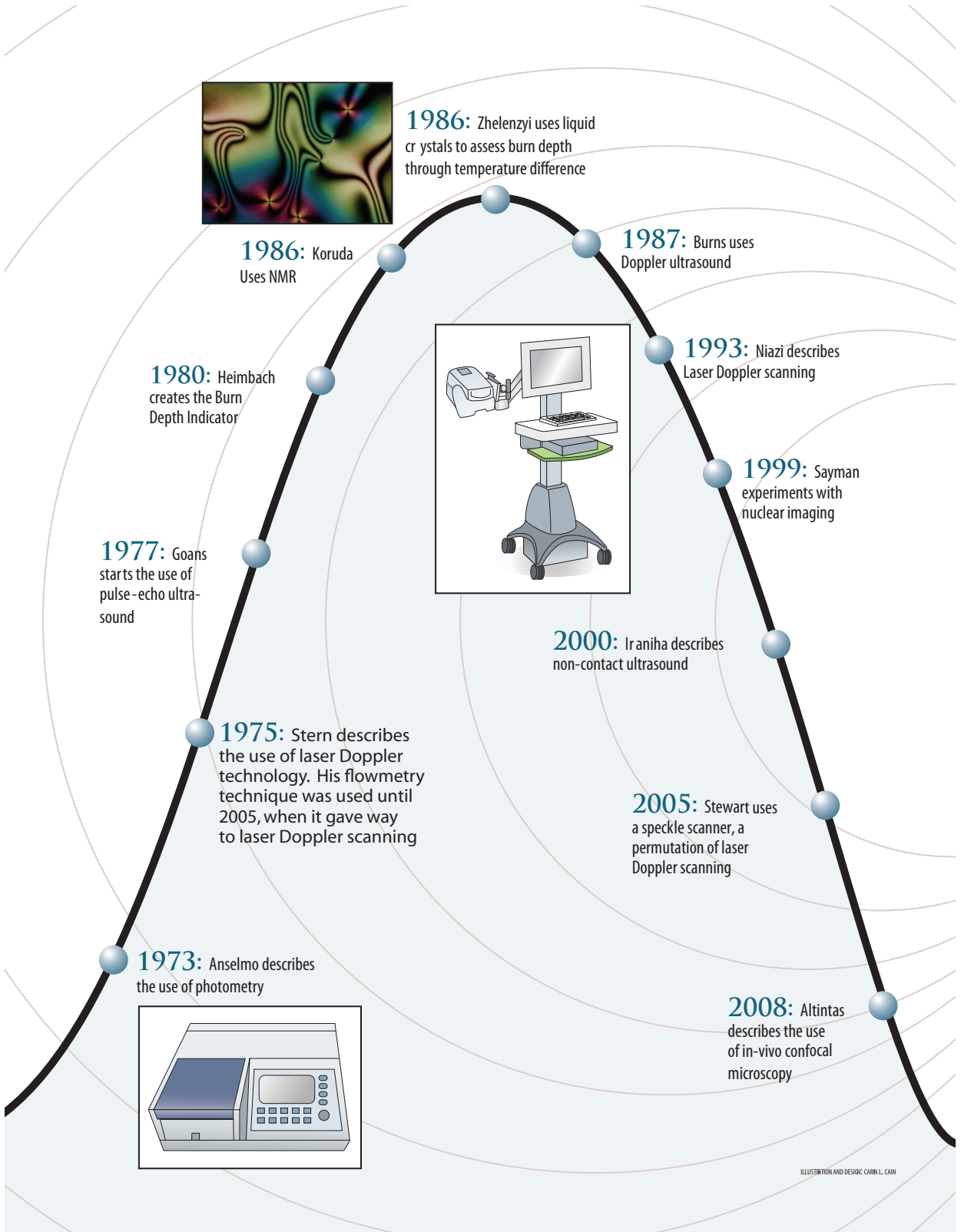
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stay and quicker return to work in those patients with indeterminate wounds treated with early excision and grafting as opposed to expectant management, albeit an increased blood product transfusion requirement.<sup>14</sup>

Through the years, there have been many modalities that have been used as adjuncts to determine the exact depth. Long regarded as the gold standard to determine exact depth, there is a wealth of literature that deals with tissue biopsies and histological analysis.<sup>15,16</sup> Through the years, hematoxylin and eosin staining has been used to determine normal and denatured collagen and the assessment of patent blood vessels has been used to mark the difference between partial- and full-thickness injury.<sup>16</sup> The addition of immunohistochemical staining techniques, such as vimentin, has also been suggested to add specificity in the acute postburn period.<sup>17</sup> The routine use of biopsies, however, becomes expensive, leaves a permanent scar, and requires an experienced pathologist, and as such are rarely used in clinical practice.<sup>15</sup> This has led some to suggest that using burn wound biopsies and histological analysis, although an important adjunct, should not be considered the gold standard for burn depth assessment.<sup>16</sup>

The need for a modality to help clinical decision making, which is less invasive than tissue biopsies has resulted in a plethora of modalities, all with mixed results. What follows is a historical account of some of the methods used with the main objective to critically assess some of the current techniques.

### Dr. Janzekovic

The idea of using excision and grafting for burn injuries is over 80 years old. Since 1928, Wells<sup>18</sup> described the idea of immediate excision followed by skin grafting to treat electrical injuries. Between the 1940s and 1950s, several surgeons used this technique of early excision, within 5 days of injury, followed by skin grafting for deep injuries.<sup>19-23</sup> The overall results were encouraging, achieving 90% graft take,<sup>20</sup> reducing contractures,<sup>21</sup> and accelerating closure while decreasing hospital stay.<sup>22</sup> Despite this, a reduction in mortality was not seen.<sup>24,25</sup> In 1970, Janzekovic described two aspects of her excision technique that would have a profound effect on the operative management of burn wounds. First, she described the importance of excising not only "extensive deep burns" but also "areas of only partial skin injury."<sup>22</sup> Second, she introduced the concept of tangential excision "to an area of profuse bleeding," rather than full excision to the level of the fascia as was performed at the time. With these changes, she noticed a decrease in mortality, pain, and infection while allowing

for a complete morphological and functional regeneration of the skin.<sup>1</sup>

The idea of preserving the dermis was not new, since in 1936, Taylor<sup>26</sup> had suggested preserving the dermis as a way to improve healing of burn injuries. This thought had been echoed by others,<sup>27,28</sup> and in 1959, Lorthioir<sup>29</sup> attempted to separate the nonviable dermis through abrasion. Difficulties in assessing burn depth and the interface between live and dead dermis limited the applicability of this thought into the excisions being performed. Between 1961 and 1969, Janzekovic<sup>1</sup> treated more than 1600 patients with her novel tangential excision method, but it was thought that the only way to assess the depth of a wound was in the operating room during excision.<sup>2</sup> A method to aid in this determination was needed.

### Radioactive Isotopes

Some of the early work regarding burn depth assessment involved the injection of radioactive phosphorus (<sup>32</sup>P). Since 1942, the detection level of <sup>32</sup>P had been studied in some superficial tissues in humans,<sup>30</sup> with an early clinical application being the detection of peripheral vascular disease.<sup>31</sup> In 1953, the discovery that uptake of <sup>32</sup>P by the skin could be quantified<sup>32</sup> led to early research in burns.<sup>33</sup> Although the animal model results were encouraging, the technique proved too cumbersome and poorly reproducible, and its use was abandoned.

### Vital Dyes

The use of vital dyes was first suggested since in 1942<sup>34</sup> as a way to assess adequacy of circulation. A year later, Dingwall<sup>35</sup> performed a series of experiments in animals and humans where he showed that full-thickness burns could be detected under a wood filter after injection of fluorescein. After this early work, the first reports of their systemic study in burns would not publish until 1961. There are two main kinds of vital dyes, nonfluorescent and fluorescent, which means that illumination of the burnt area with ultraviolet light can detect the presence of the dye at specific depths.

Among the nonfluorescent dyes, some of the earliest reports used bromophenol blue,<sup>36</sup> and patent blue V.<sup>37,38</sup> Because these two agents were not approved for clinical use, the only studies performed were in murine models. Both, bromophenol blue and patent blue V were able to differentiate necrotic from living tissue on the surface.<sup>39</sup> While exciting at first glance, this is not enough because no determination of the depth of necrosis can be made. To avoid this problem, fluorescent dyes were attempted.

The earliest fluorescent dyes studied were fluorescein<sup>40,41</sup> and tetracycline,<sup>42</sup> which had the added ad-

vantage of being approved for clinical use. Different dosages and times of injection were suggested in the case of tetracycline and early reports suggested that different depths of skin necrosis were distinguishable to some extent.<sup>39</sup> This was, however, a fixed distance from the surface in millimeters and did not account for the skin having different thickness in different parts of the body. In the case of fluorescein, some reports suggested that ultraviolet light was not an absolute necessity for some differentiation of depth.<sup>41</sup> The main problem is that no quantification method could be developed and, as such, it remained no better than clinical judgment. Despite this, it has been used intraoperatively as an adjunct in difficult cases or critical areas such as the hands.<sup>43</sup> The development of a fluorometer in the late 1970s allowed for quantification of the fluorescein within a tissue.<sup>44</sup> Studies assessing both delivery<sup>44,45</sup> and extraction<sup>46-48</sup> of fluorescein from tissues allowed for some degree of quantification of blood flow, and initial studies in burn patients were encouraging.<sup>49</sup> However, a follow-up study confirmed the fact that the variability of the readings was large and as such, it did not provide a definitive assessment of the depth of the wound surveyed.<sup>50</sup>

The most recent fluorescent dye to be studied is indocyanine green. Initially described for assessment of burn depth in an animal model in 1992 by Green et al,<sup>51</sup> the initial animal<sup>52,53</sup> and human trials<sup>54,55</sup> have shown potential value. The fact that the contrast is extravasated in the period of capillary leak<sup>56</sup> limited clinical application initially, although a recent report suggests improved detection capabilities with indocyanine green video angiography.<sup>57</sup>

## Thermography

One of the earliest adjuncts to clinical judgment to assess burn depth was thermography, the science of recording graphically temperature, or changes in temperature. Machines capable of determining a difference in skin temperature as small as 0.1°C were developed in the 1950s and 1960s and their use adapted to clinical conditions such as detection of tumors<sup>59,60</sup> and the viability of pedicle flaps.<sup>61</sup>

With respect to burns, the theory was that deeper injuries would be appear colder than more shallow ones owing to a decreased perfusion.<sup>60</sup> Early work in the 1960s suggested that this was indeed the case,<sup>62</sup> and follow-up work suggested that the difference between partial-thickness and full-thickness wounds was about 2°C.<sup>63</sup> Hackett<sup>64</sup> performed one of the largest studies in burn patients in 1974, surveying the wounds of 109 patients and found a 90% accuracy in the assessment of depth using thermography based

on the determination of a 1°C difference in temperature between the burn wound and the intact tissue.

Further work by Anselmo and Zawacki revealed some of the pitfalls of this technology. In an animal model, they showed that evaporative loss of heat, or evaporative cooling, could disguise the temperature differential of a partial-thickness wound and lead to a false diagnosis of a full-thickness one. Similarly, a full-thickness wound with an intact blister could conserve enough heat to lead to a false diagnosis of a partial-thickness wound.<sup>65</sup> These drawbacks seemed to be more evident within the first 4 days after injury. Although the technique continued to be used in Poland and Russia,<sup>66-71</sup> elsewhere it fell in disuse until 1990s when Cole et al<sup>72</sup> used cling film (Saran wrap™) to eliminate evaporative cooling. Using this technique, they correctly predicted either healing or need for excision and grafting in 33 of 36 wounds, whereas clinical judgment was accurate in only 22 of 36 wounds.<sup>73</sup> Despite the use of a barrier method to decrease evaporative cooling, the best time to perform thermography seems to remain at 72 hours postinjury.<sup>74</sup>

One important aspect to note is that each study published seems to have a different cutoff point in terms of the temperature difference needed to consider a wound full thickness. A recent study by Renkielska et al<sup>75</sup> supports this and underscores the importance of each center, validating their own values for burn classification; that is, at what temperature difference from normal skin is excision necessary. Ongoing work using newer thermography modalities, such as active dynamic thermography<sup>76</sup> and infrared (IR) thermography,<sup>77</sup> suggest an advantage in this aspect to traditional static thermography. Briefly stated, rather than assessing the temperature difference between injured and noninjured skin, this technology relies on the difference in conductivity and thermal diffusivity between burnt and nonburnt tissue. After obtaining a baseline reading on the temperature distribution of the tissue in question (with the standard IR cameras), the tissue is heated with halogen lamps (external thermal excitation by optical irradiation), followed by measuring the temperature changes. Initially described in 1999,<sup>78</sup> this technique has been tested using phantoms and correlated to histopathology in an animal model.<sup>76,79</sup> A pilot study on normal human volunteers shows promise,<sup>80</sup> but the results are too early to draw conclusions of its eventual usefulness in burn patients.

## Photometry

Anselmo and Zawacki<sup>81</sup> first used photometric techniques in 1973. Their rationale was that infrared light

could be used to differentiate open from thrombosed vessels, ie, superficial from deep burns. In their initial study, they proved that computer-enhanced images could differentiate between superficial and deep wounds, and in a follow-up study<sup>82</sup> they automated the process even more by taking pictures of the burn wound using green, red, and infrared light and then “subtracting” the surface features seen with the green and red light from the infrared detected image. Their studies paved the way for Heimbach et al<sup>83</sup> to develop a “burn depth indicator” in 1980. Briefly stated, their apparatus consisted of a probe lined with light-emitting diodes that could emit green, red, and infrared light, as well as detect the intensity of the reflected light. The output was a computation of the different ratios of reflected light (ie, green-IR, red-IR, green-red). They validated this burn depth indicator against the clinical judgment of two senior burn surgeons and found it to have a better negative predictive value, ie, better than clinical judgment at determining which wounds would not heal spontaneously within 3 weeks. It was also better at predicting healing in those wounds that the surgeons thought they could not exact an opinion.<sup>12</sup> Further refinements of this technique have yielded a color palette, more user friendly than the ratios of reflected light, and which characterizes the wounds into likely to, unlikely to, and definitely not going to heal within 3 weeks.<sup>84,85</sup>

### Assorted Modalities

**Liquid Crystal Thermoindicating Film.** Because of the difficulty of the problem, and the lack of one measurement technique that stands clearly as the best, a multitude of other techniques have been attempted. One such technique was the application of liquid crystal thermoindicating films directly on the wounds of humans to measure the temperature of the burn wound. Although similar in concept to thermography, a colder measurement signifies a deeper wound, the results in this study were too unreliable.<sup>86</sup>

**Nuclear Magnetic Resonance.** With the advent of nuclear magnetic resonance, Koruda et al<sup>87</sup> used this technique in an animal model to assess burn depth. This was based on the fact that there is a differential edema resorption time between partial-thickness (faster resorption) and full-thickness wounds (slower resorption). Because the T1-weighted images correlate strongly with total water content in the tissue, sequential images could be used to differentiate partial- from full-thickness injuries based on the change in water content. Although their study proved that indeed nuclear magnetic resonance can differentiate between partial- and full-thickness burns based

on the water content, the fact that total water content was measured in vitro by desiccation limits the clinical applicability of this study. Animal work suggests that there are in vivo ways of establishing this difference, but the results are still too early to establish conclusions.<sup>88</sup>

**Nuclear Imaging.** After its application for assessment of muscle damage/myonecrosis after electrical injury, the injection of radio-labeled tracers to assess the patency of the microcirculation at the area of thermal damage was attempted. An animal model using <sup>99m</sup>Tc (methoxyisobutylisonitrile) showed decrease tracer uptake in the area of injury.<sup>89</sup> Considering the wealth of noninvasive modalities that can also provide a faster assessment, the clinical applications of nuclear imaging seems impractical.

### Ultrasound Techniques

**Pulse-Echo Ultrasound.** During the 1970s, ultrasound was becoming more widely used in a variety of applications in medicine. The study by Goans et al<sup>90</sup> on animals suggested that ultrasound could be used as a quantitative method of assessment of burn wounds. The idea was to identify the interface between the coagulation necrosis layer and the remaining viable dermis. Similarly, it could detect the interface between the deep dermis and the subcutaneous fat, thus giving a measurement of the remaining dermis. After this rationale, Kalus et al<sup>91</sup> used a 5-MHz probe in two patients, accurately predicting healing in one of them and the need for excision in the other. The advantages of ultrasound as a noninvasive, expedient way to help determine burn depth were echoed by others in animal models.<sup>92,93</sup> Improvements in technology brought improved images in animal models as probes went to 10 MHz<sup>94,95</sup> and 18.5 MHz,<sup>96</sup> and in humans for the assessment of other skin conditions such as melanoma and psoriasis<sup>97</sup>; however, these results did not translate into similar results in humans suffering from burn injuries.<sup>98</sup> A potential reason is that some of the animal studies differentiated between normal and denatured collagen and not epidermal cells. This is important for while collagen denatures at 65°C, the epidermal cells do so at 47°C. It is possible then that ultrasound underestimates the real depth of injury.<sup>15</sup>

**Pulse-Wave Doppler Ultrasound.** The addition of Doppler images in the mid-1980s to traditional B-mode ultrasound added an important element to the morphologic information obtained. Briefly stated, the Doppler principle states that a wave form aimed at an object will bounce off it and return unchanged if the object is static, but will return with a deflection if the object is in motion. By measuring the degree of this deflection, the velocity of the object is known. Al-

though ultrasonic Doppler provides velocity information without depth resolution, the addition of pulsed Doppler to real-time B-mode ultrasound provides, in theory, a more robust assessment of depth and viability of a wound.<sup>99,100</sup> Early animal work showed that indeed high-frequency Doppler ultrasound (50–200 MHz) could detect *in vivo* velocities in the order of those expected for blood within the capillaries.<sup>101,102</sup> One human study testing a noncontact, pulse-wave Doppler ultrasound found a 96% correlation between ultrasonography and the prediction of healing within 3 weeks.<sup>103</sup> As important as this finding was, Doppler ultrasonography would not last, giving way then to a new technology: laser Doppler.

### Laser Doppler

The first suggestion of the use of laser Doppler flowmetry for the evaluation of burns dates from 1975, when Stern<sup>104</sup> described using a 632.8-nm helium–neon laser to assess the circulation of a fingertip following different conditions. His initial experiment showed that the velocity of moving particles could be assessed and that the number of moving particles could be derived as well. Finally, he showed how the output measurement was quite labile as it was affected by room temperature, patient position, respiratory pattern, and even emotional stimulation. Nevertheless, this provided a noninvasive way (although contact with the skin was required in this initial description) to assess rapid changes in perfusion in a specific area. Two more reports followed, assessing the feasibility of measuring superficial blood flow under a variety of conditions in both animals<sup>105</sup> and humans,<sup>106</sup> eventually leading to the first systematic series of studies in burn patients in 1984 by Micheels et al.

In their first study, Micheels et al<sup>107</sup> confirmed Stern's observations of being able to assess microcirculation over a variety of physiologic conditions. Their follow-up study tested the ability to measure microcirculation in a burn wound and the ability to measure the effect of vasodilatation.<sup>108</sup> They showed a correlation between the clinical assessment of burn depth and the local blood flow. In their final study,<sup>109</sup> they scanned 15 burn patients on the third postinjury day and compared the measurements from the laser to clinical judgment and wound biopsies. They found that the laser Doppler correlated closely to histology and was superior to clinical judgment. It is important to note that this study did not look at the natural history of the scanned wounds, and no prediction of healing within 21 days was made.

The first observational study correlating laser Doppler measurements with potential of healing of

wounds was performed by Green et al.<sup>110</sup> This was an observational study in which the authors noted an increased perfusion in those wounds that eventually healed without the need for grafting than in those in which excision and grafting were necessary. In reports that followed, several investigators claimed laser Doppler predicted healing within 21 days with 70 to 100% accuracy<sup>111,112</sup> and failure to heal between 93 and 100% accuracy.<sup>111,113,114</sup> These results have also been confirmed in children<sup>115</sup> and also specifically in the hands, where the expected time to heal is only 14 days.<sup>116</sup>

Although all of these results were encouraging, two main problems remained with the laser Doppler flowmetry technique. The first was that there had to be contact between the laser and the tissue, and the other, partly related to the close contact, was that only a 1-mm area could be studied at a time. To circumvent these pitfalls, Niazi et al<sup>117</sup> described and studied a laser Doppler scanner in 1993. The patients could be as far away as 1.6 m from the scanner, it allowed the study of a 500 × 700 mm area in 6 minutes; and, most importantly, there seemed to be a good correlation between the scans and the clinical outcome of the wounds. Correlation between laser Doppler scanner (or laser Doppler imaging) and time to heal was confirmed independently by Pape et al<sup>118</sup> and Kloppenberg et al<sup>119</sup> in adults and by Holland et al<sup>120</sup> in children. A study by Jeng et al<sup>121</sup> suggested that not only it could predict healing potential but also that it could do so 2 days ahead of clinical judgment.

A very important finding from the study of Kloppenberg et al was that wounds of different depths, superficial second, deep second, and third degree all behaved differently when scanned on successive days. The most superficial wounds started with a high perfusion and proceeded to decreased perfusion on successive scans during 2 weeks. Wounds of intermediate depth also started with a high perfusion and progressed to an even higher value after 4 days, eventually declining. The deepest wounds started low and stayed low. In light of these findings, several questions arise about laser Doppler scanning. The first is how consistent are the measurements? When Stern described the technique 26 years earlier, he noted that the measurements were quite labile, being affected by a variety of factors, both environmental and physiologic.<sup>104</sup> The fact that laser Doppler provided such an automatic measurement of flow was initially seen as a very positive aspect. However, in a dynamic environment such as a burn, the numbers then need to be followed carefully. Furthermore, what is the effect of changing basic conditions, such as the distance from the wound, the room tem-

perature, and the angle at which the scan is being performed on the output measurement? And a third question, if the laser Doppler measurements are so sensitive to external conditions, and a burn wound is such a dynamic environment in the first few days after injury, when is the best time to scan? The answers to these questions are fueling the current research efforts with regard to laser Doppler scanning and will ultimately decide the fate of this technology.

### Newer Technologies

As the problem of accurately assessing burn depth continues, newer technologies are being developed. Recently, there has been excitement with the development of speckle technology as the next step in the evolution of laser Doppler scanning. Also recently reported is the use of *in vivo* confocal microscopy to assess burn depth.<sup>122</sup> Both of these technologies are very new and, as such, it is too early to provide a critical assessment.

### SUMMARY

Multiple techniques to assess burn depth and to try to predict time to heal have been used in the last 70 years. In an evidence-based medicine environment, the question of the level of evidence arises. The Committee on Organization and Delivery of Burn Care defined class I evidence as “a prospective, randomized controlled clinical trial in which an investigational treatment plan is compared to existing standard therapy, using a defined endpoint including costs, risks, and benefits.”<sup>123</sup> According to this definition, most of the current evidence is class II or class III (Table 1). Furthermore, comparisons between studies are difficult as most used different methodologies and end points.

The problem of burn depth assessment to guide clinical decision making is as ever present today as it was 70 years ago. Certainly, there has been progress and the “questionable” wounds are but a subset of what they used to be. In an immediate gratification world, we expect to know immediately how a wound is going to behave. There is a certain frustration in the realization that the definition of which wounds are expected to heal seems to be a moving target. No one technology has emerged as the gold standard, the time that it takes for a wound to heal and the quality of the end-result continue to guide clinical decision making. We now have a better understanding of some of the factors that influence burn wound healing. A wound is a very dynamic process in the first 48 hours

**Table 1.** Level of evidence for the different technologies used to estimate burn depth following the definition of classes of evidence provided by Gibran<sup>123</sup>

| Technique                            | Level of Evidence                           |
|--------------------------------------|---|
| Radioactive isotopes                 | Technology assessment<br>Animal work        |
| Nonfluorescent dyes                  | Technology assessment<br>Animal work        |
| Fluorescent dyes                     |   |
| Tetracycline                         | Class II                                    |
| Fluorescein                          | Classes II and III                          |
| Indocyanine green                    | Class II                                    |
| Thermography                         | Class II                                    |
| Active dynamic thermography          | Technology assessment                       |
| Photometry                           | Class II                                    |
| Liquid crystal thermoindicating film | Class III                                   |
| Nuclear magnetic resonance           | Technology assessment                       |
| Pulse ultrasound                     | Class II                                    |
| Doppler ultrasound                   | Class II                                    |
| Laser Doppler imaging                | Technology assessment<br>Classes II and III |

after injury; perhaps, expecting any one of these technologies to “predict” healing during this time period is illusory.

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