

Imaging and Measurement

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# Imaging and Measurement

Jacopo Secco

**Abstract** Imaging and measurement have always been two of the most important procedures of medicine nowadays. Obviously the techniques to perform these procedure have evolved over time and nowadays new and more sophisticated tools in the aid of diagnostics are developed daily. Here we will treat and describe the techniques that are implemented and that are being developed in the treating of chronic wounds. Their importance has become even greater due to recent events such as COVID-19 pandemic which has shed light on the high necessity of procedures that can aid physicians and nurses in treating ulcer patients remotely maintaining the highest standards of cure possible. As said, developments are still ongoing setting higher goals regarding diagnostic precision and efficiency of cure, and it is demonstrated how all the solutions that have reached the clinical use have opened the pathway for the most recent or future innovations in this field.

## 1 Introduction

As in all medicine research fields, the importance of a newly developed solution is *measured* through the gravity of the problem. Regarding chronic wounds, it is a fact that kin ulcers are a chronic pathological condition affecting around 1 – 2% of the world's population [1]. In Europe alone, over four million patients are affected by this syndrome, costing €4 billion in national health treatment every year. Primarily found in people > 65 years of age (> 60%), skin ulcers are commonly associated with pre-existing chronic diseases such as diabetes, vascular problems, heart disease and obesity [2]. Early detection and assessment of the wound is vital; after four weeks there is a 30% chance of the lesion never healing, a 50% chance of loss of limb and a 50% chance of mortality in the following five years [3].

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Jacopo Secco  
Politecnico di Torino, Department of Electronics and Telecommunications, Corso Duca degli  
Abruzzi 24, 101023, Torino, e-mail: jacopo.secco@polito.it

Chronic pain, reduced mobility, and psychological and emotional stress are just a few of the difficulties commonly experienced by patients with this skin condition.4 Furthermore, treatment of skin ulcers may prove lengthy, taking several months or even years for the wound to heal [4]. In many patients, complications arise that require urgent surgical intervention leading to long periods of hospitalisation [5].

From the presented data it is clear that there is the need in common clinical practice regarding chronic wounds of tools that can assist the care-givers in delivering the required amount of assistance o their patients. A recent study has shown that through the use of medical devices and standardized procedures that helped the physicians and the nurses simply to communicate more efficiently the results of the delivered cures has substantially increased the healing rate from 75% to 90% of the overall cases. The same study has also demonstrated that the same approach has lead to a decrease of the cost of cure by 35% due to more precise prescriptions and an increased control on the cure plans [6]. These results are surely encouraging and are the outcome of the last 20 years of research in the field [7].

From the work of Bekara *et al.* [7] and from even a more recent review on the new wearable technologies for ulcer management and assessment by Wang *et al.* [8], it is clear that the keywords are essentially two: *measure* and *communicate*. Obviously the first leads to the second, but it also sub-intends another essential requirement: *standardization*. In this last decade the world of medicine has seen great technological evolution, not only regarding diagnostic means, but also regarding methods of transmitting the information remotely and in a precise fashion. The birth of telemedicine and its conquest of a fundamental role in future diagnostics and patient care due to the COVID-19 pandemic taught a valuable lesson not only to the care-givers, but also to the whole hospital management community [9, 10]. In order for this to happen it is crucial that the information that is gathered from a patient must be extremely precise and complete in order to perform the best possible assessment.

Leading the discussion back to ulcer cure, one of the fundamental milestones that technological assessment has reached is the standardization of the clinical information regarding the assessment. Quantification in wound care is a grey area in which many works have been published but authors have yet to reach a consensus. A number of parameters are measured. The work of Mani *et al.* remains one of the cornerstones, listing the various measurement possibilities [11]. The pH is intended to be an indicator of tissue repair, considering also its role in the microenvironment of the wound bed [12]. Transcutaneous oxygen and flow at the microcirculatory level are important, but only as indicators of possible results in terms of tissue vitality. The fact that a skin ulcer has a defined area and volume, although not simply measured, has led many authors to further investigation. For clinicians, the objective of measuring is to be able to better define the evolution of a wound, whether it is being repaired, blocked or worsened; Flanagan *et al.* define wound reduction parameters as repair indicators [13]. Sheehan *et al.* have demonstrated that, in the case of diabetic ulcers, early assessment (within four weeks) is crucial for full recovery [3]. Gorin *et al.* have analysed the reduction of wound area, width and length, and concluded that a linear parameter is independent of the geometric shape of the wound [14]. Cukjati *et al.* reiterate how wound area and its variations indicate evolution and prognostics [15].

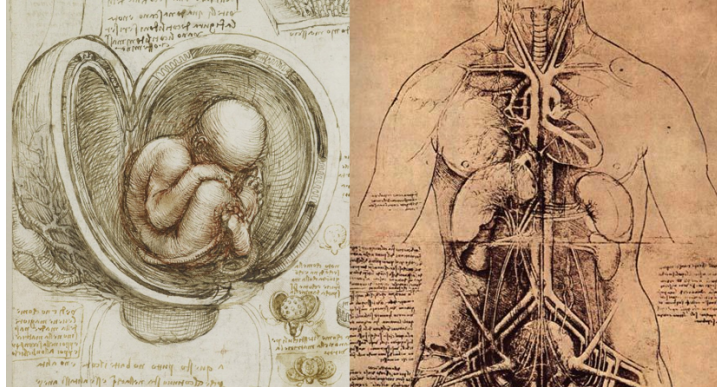
Moreover, the percentage change of the wound area is a clinically recognised prognostic measure, although the problem remains of how to measure it [16, 17]. Wound area is not the only prognostic indicator. Solutions have been developed that propose a subdivision of the lesions—in terms of tissue type and exudate management may be considered an appropriate indicator of clinical results. One of the most commonly used is the Wound Bed Preparation (WBP) score proposed by Falanga as an analysis parameter as it is well known and used on different types of wounds [18].

As shown, ulcer assessment can take into account many different variables, and an accurate relation amongst them can surely lead to an always more complete wound classification in diagnostic terms. In any case as mentioned by Khoo *et al.* and by Haghpanah *et al.* the capability to perform a correct morphological measurement of the wound, and its variations, in its healing process is one of the key elements for a correct diagnosis. In these terms the evolution in wound treatment techniques has been followed by a parallel evolution of the imaging and measurement devices for wound treatment [19]. Just in the last ten years different solutions have been developed, trialed and brought to the market, entering one by one in the standard procedures for wound treatment, always increasing their efficiency and precision. The following sections will deliver an overview of both imaging and measurement techniques used in wound care nowadays, due to their proven diagnostic significance. The devices and the procedures that are here described set the actual standard of cure and show a glimpse of the future of this always developing field. The final goal, is to give a better understanding of the future of wound assessment and how technology can help the care-givers, which are always working in the front line, to render an always higher standard of cure meeting the ongoing life and social requirements.

## 2 Overview on Imaging Technology in Wound Care

In order to measure something it is necessary first to *feel* it, or even better, to *see* it. Historically seeing something under the skin has been one of the major problems to overcome. At first physicians were obliged to look for different symptoms by touching the patient, searching for cutaneous eruptions, rashes or wounds, or even to auscultate the body by laying the naked ear on the patient's skin. These methods were the only available until the 18<sup>th</sup> century for obvious reasons. The main, and probably the only, reason was that it was thought to be unnecessarily dangerous to cut open the skin to simply look inside the body unless no other solution was possible. As a matter of fact instant cauterization techniques such as the electric scalpel did not exist until the 1920s. For this reason the first studies of the human anatomy and physiology in Europe were conducted by dissecting dead bodies. Moreover the first anatomists had also to have an outstanding artistic talent since all their observations had to be hand drawn for future studies. Two of the most famous artists and anatomists lived between the end of the 15<sup>th</sup> century and the first half of the 16<sup>th</sup> and were Andreas von Vesalius (a.k.a. Andreas Vesalius) and Leonardo da Vinci, whose some

of their studies arrived to us as true pieces of artwork (two examples of Leonardo's anatomical work are shown in Figure 1).

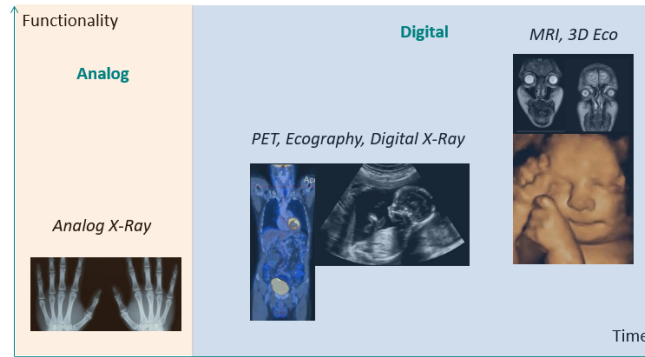


**Fig. 1** Two examples of Leonardo da Vinci's anatomical work. It is known that the famous Italian artist used to buy corpses from the dead person's families in order to dissect them and draw his observations. Amongst the many interests of Leonardo, was also medicine at his ateliers.

In the eighteenth-century two major discoveries gave birth to what today we call *medical imaging*. The first was the invention of photography in 1827 by Nicéphore Niépce in collaboration with Louis Jacques Mandé Daguerre. The second was the invention of X-ray tube by Wilhelm Röntgen. The evolution of these techniques has led to the birth of the field of medical imaging. This field has become so popular and so important that it is reported that by 2010 around 5 billion medical imaging studies have been conducted worldwide, and it is estimated that by 2020 these have increased by 10% [20].

Medical imaging started to have a greater differentiation between its morphological and functional purposes with the advent of digital images in the 1990s. At first all imaging techniques, not only in the medicine field, were analog. This meant that the resulting image from a camera, an X-ray machine or whatever imaging device, imprinted directly the subject of the representation on a portable physical medium. Common cameras used film rolls made of celluloid, same as the X-ray machines that initially exploited celluloid films with silver ions that had a direct reaction with the ionizing radiation passing through a body. Digitalization permitted to convert the image in a series of *bits* (i.e. digits, 0s and 1s) through silicon-based sensors. The obtained data can be easily stored in semi-conductor based memories such as the memory of an electronic device, and can be directly analyzed using both simple and complex mathematical models. The capability of digital images to be both visualized and analyzed has increased the functionality of medical imaging. For instance a defect detected from an analog X-ray image could not be easily measured in its size, and comparisons on the same defect detected from two different X-ray machines could not be easily performed unless the same defect presented great variations. On the other hand, thanks to the Computerized Tomography (CT) which

is a digital X-ray machine capable of scanning the whole body dividing it in slices, it is possible to digitally reconstruct in 3D the same defect measuring it in all its dimensions. From a time-development perspective, parting from the point that a first digital transformation of medical imaging devices occurred, the spectrum of functionalities that can be achieved through medical imaging devices has become exponentially greater (an example is shown in Figure 2).



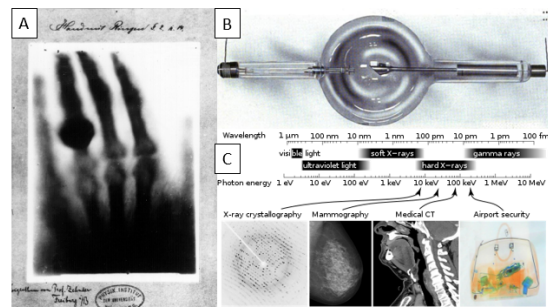
**Fig. 2** The figure shows a time-functionality development graph with different examples of imaging techniques. From the advent of digital imaging the diagnostic functionalities that can be obtained from an image have increased exponentially. As shown in the figure, traditional X-ray images have been the state of the art of diagnostics for many years: by converting the image in digital form, imaging devices can perform complex analysis directly on the obtained data.

In wound care, obviously, imaging serves as a powerful tool not only in representing the wound *per se*, but also aiding the physicians and nurses to have a better understanding of the ulcer evolution. As mentioned in Section 1 wound care specialists have a need of more efficient instruments and devices in order to correctly capture the features of the lesion. These feature are different and not always visible to the naked eye. Digital imaging aids the specialists in different ways, depending on the clinical parameters that are needed to be gathered. Not all the imaging techniques are commonly used in this particular field of medicine due to several factors such as the etiology of the wound, the presence of required equipment, and the actual need of distinguishing different clinical features. In any case all the means that are nowadays used permit physicians and nurses to perform specific and precise measurements and analysis increasing the standard of care and consequently its healing efficacy. As mentioned, depending on researched clinical feature, different technologies can be exploited. These can be subdivided in two main groups that will be treated in more detail in the following subsections: *optical* and *non-optical* imaging.

## 2.1 Optical Imaging in Wound Care

In general optical imaging is the branch of imaging that exploits light at different wavelengths to generate an image. Different wavelengths (i.e. visible, IR, X-ray, and others) can enhance or filter certain features or objects in the final picture. The most renowned optical imaging technology in the medical field is the X-ray. Discovered by Wilhelm Rontgen, who consequently invented the X-ray tube, in the late eighteenthundreds this technology permits to see through the soft tissues of the body by emitting high energy photons (with wavelength between  $1\text{nm}$  and  $1\text{pm}$ ). Figure 3 shows in A - one of the first X-ray images taken by Rontgen (his wife's hand with the wedding ring visible), B - an example of the X-ray tube, and C - the wavelength spectrum of X-ray light. In principle the X-ray tube is a glass ampoule under high vacuum that contains a cathode and a high-voltage anode. The cathode (or negative pole), as in ordinary thermionic valves, in turn consists of the heater filament and the actual cathode, which is connected to the high-voltage circuit. The filament usually consists of an alloy of copper or other metals with low atomic number, and is powered at low voltage; the anode (positive pole), on the other hand, located at the opposite end of the ampoule, consists of a disc (plate) of heavy metal (with high atomic number, such as alloys of tungsten and molybdenum for conventional diagnostic tubes, molybdenum or rhodium for tubes used in breast diagnostics), which can be fixed or rotating. Rotation allows for better dissipation of the heat formed on it, which reaches temperatures on the order of  $2000\text{ }^\circ\text{C}$ ). X-ray generation occurs by *Bremsstrahlung* [21] (braking radiation) and by characteristic radiation. In modern tubes, the metal disk at the anode is rotating: this expedient lengthens the life of the tube by preventing electrons, always hitting the same spot, from prematurely eroding the electrode ("cratering" of the anode) and improves its image sharpness. Rotation of the anode also allows for better thermal dissipation, as it provides a larger surface area for electrons to impact.

**Fig. 3** A brief summary of the X-ray functioning. A - The famous X-ray taken by Wilhelm Rontgen himself: the image shown the hand of Rontgen's wife with the wedding ring. B - The X-ray tube. C - Wavelengths and some examples of X-ray uses.



As already mentioned in Section 2, also the X-ray devices have passed a process of digital transformation. Until a few decades ago, this generally consisted of photographic film coupled with a reinforcing screen that could impress X-rays passing through the patient's body. Nowadays with the advent of digital radiography, the film

has been replaced by X-ray cassettes containing photo-sensitive substances that will then be read by appropriate sensors and display the resulting image on a monitor. In more modern systems, an array of scintillators and Charge Coupled Devices (CCDs) are able to acquire images directly. With Digital X-ray it became possible to perform analysis directly on the image: these analysis can include the measurement of tissue morphology (also in 3D if the images are taken with a CT device) or the intensity of the given signal. An example of the last case are angiographies or in other words X-ray images of vascular districts of the patient. Through the use of a contrast (i.e. a liquid that is injected directly in the patient's circulatory system) capable of partially reflecting photons emitted by the machine, it is possible to obtain reliable and live data on the hematic perfusion, which is one of the most crucial indicators of the insurgence or the healing of chronic wounds.

Due to the limitations of X-ray imaging, the most commonly used technique in everyday wound care practice is what is called *Enhanced Digital Imaging* (EDI). Usually EDI devices consists of a normal Complementary Metal-Oxide Semiconductor (CMOS) digital camera that, with some exceptions, works in the visible light range. These sort of devices allow the operator to take a normal digital picture of the wound and through different techniques the care-giver can perform several analyses on the lesion, such as classifying the different tissues or perform morphological measurements and comparisons between different healing stages.

As for the production of an X-ray image, visible light digital cameras can transform the intensity of reflected light from different parts of a scene. The element capable of performing this function is the sensor, which has a different form depending on the type of camera. The function that the sensor performs within a digital camera is analogous to what film does in traditional photography. From this it is easy to understand how the optical part of focusing the image on the surface of the sensor retains a central role in digital photography, being responsible for the resolution of the images obtained and contributing to their quality. As afore mentioned digital cameras implement a photo-sensitive sensor that is responsible of transforming the analog signal of the input light into digital data. An active-pixel sensor (APS) is an image sensor in which each pixel sensor unit cell has a photodetector (typically a locked photodiode) and one or more active transistors. There are several types of APS, including the early APS NMOS and the much more common CMOS. The CMOS sensor is composed of photosites that is the smallest space within an imaging sensor with one or more photosensitive semiconductor elements capable of transforming a light flux into a given amount of electrical charges. In the photosite, in addition to the sensing element, there is usually a microscopic optical system overlying the photodetector consisting of a small crystal with a quasi-spherical dome shape having the function of capturing as much light as possible of that incident on the sensor surface. Sometimes this crystal (or transparent resin) is an "R" or "G" or "B" colored unitary element of the Bayer filter, the so-called Color Filter Array (CFA). The photosite is also the unitary part of a larger place that is generally called a sensor. The characteristics of the photosite make it possible to understand, both electrically and optically, how the individual image-forming elements are captured.

EDI's implementing simple CMOS cameras presume several favourable functional elements that render them the most commonly used devices in wound care. The main element is the simplicity of the technology: CMOS sensors can be very small and its technology has become extremely reliable and standardized under an implementation point of view. These sensors can be built on portable devices, do not require high energies to work and their configuration has become extremely simple and cheap for the device-producing companies. The second advantage of the CMOS sensors is their functioning reliability. As reported the sensors are neatly organized through their photosites that subdivide the image into small basic and regular elements known as pixels. Through simple mathematical transformations it is easy to determine precisely the physical surface that is depicted inside a single pixel of a picture. By knowing this piece of information, performing reliable and precise measures of the subject of a photo (for instance a wound) has become easy and fast. Moreover, as in the case of the X-ray machines, having the same reference, it is consequently possible and easy to compare the size variations of the given subject with a high fidelity throughput.

There is one last advantage that is given by the use of the EDIs: the standardization of the color patterns of the image. As in all digital means of depiction, the image is given by the direct transformation of the light intensity that hits the sensor into a digital signal. With the same technique colors are rendered by filtering the three main color components: Red, Green and Blue (RGB) through the Bayer filter of the photosite. This has become a great advantage in image analysis in wound care since color can be taken as a primary feature in order to distinguish the different tissues of a wound. If we take for instance into consideration the work of Falanga *et al.* [18], it is possible to exploit this feature in order to perform a classification of the wound through the WBP score regarding granulation. In the last ten years, different EDIs have hit the market and have been integrated in the good clinical practice in wound care. These devices can also implement other collateral sensors and emitters in order to perform other kinds of measurements (i.e. laser emitters or Infra-Red IR type-C LEDs for the non-invasive measurement of the depth of the lesion). Thanks to the correct scaling of the digital picture of the wound these device can permit a manual tracing morphological measurement [22]. In other cases, exploiting the capability of standardizing the colors schemes of the wound, and through the use of advanced artificial intelligence algorithms, EDIs can be also capable of performing completely automatic measurements and correct clinical wound classifications [23]. The methodologies implied in wound measurement and assessment will be described in depth in the following sections of this chapter.

One last mention in the class of optical imaging technologies must be given to Hyperspectral Imaging (HI). This kind of imaging is usually performed with EDIs that also implement emitters of light at different wavelengths. These emitters are installed on EDIs since the emitted photons are not considered to be at high energy as the X-ray. Moreover the reflected light (i.e. the light generated by the photons that are reflected from the surface of the illuminated skin portion) can be easily seen through optical filters or through specific sensors depending on the cases. HI devices are used for several scopes in wound care such as the analysis of the

blood oxygenation of the peripheral districts or to evaluate the presence of possible infections or inflammations. Summarizing, considering the most commonly used HI technologies, it is possible to distinguish three different techniques and their use depends on the distinguished wavelength of the emitted light.

1. **Near Infra-Red Spectroscopy (NIRS)** is a non-invasive functional technique that employs scattered light in the near-infrared spectral band to investigate the hemodynamic activity of a given body district and its associated functional capacity. It is usually used in the field of neuroimaging, but in recent years it has been exploited also in the field of wound care. NIRS allows the quantification of chromophores concentrations as a result of absorption and scattering phenomena related to scattered light in the near-infrared electromagnetic spectrum (wavelengths between  $700nm$  and  $1mm$ ). In this case, the chromophores of interest are represented by the contributions of oxygenated and deoxygenated hemoglobin at the most superficial areas of the cerebral cortex. In fact, the absorption coefficient of water (the main constituent of biological tissues) within this spectral band is negligible compared to those for hemoglobin. Therefore, measuring differences in the absorption spectrum over time makes it possible to attribute almost entirely measured changes in light intensity to respective changes in hemoglobin concentration. Conventionally, at least two different wavelengths are used, one above and one below the isosbestic point between oxygenated and deoxygenated hemoglobin within the near-infrared spectral band; however, it is possible, both theoretically and experimentally, to employ multiple wavelengths in order to achieve better discrimination of the concentrations thus measured or, likewise, to investigate the trend of additional chromophores [24].
2. **Ultraviolet radiation for bacterial fluorescence** is a technique that exploits low intensity UV light (between  $315nm$  and  $400nm$ ) in order to trigger the fluorescence phenomena of certain bacterial strains that can proliferate in the wound bed. In [25] it is described a new generation device (the Moleculight™) which exploits this phenomenon and has shown the ability of obtaining high standard results with bacterial detection and differentiation in wounds. These device implements a Wood's Lamp or black light which is a light source that emits electromagnetic radiation mainly in the UVA range and to a negligible extent in the visible light range. The Wood's Tube Lamp, unlike ordinary fluorescent tubes, does not employ phosphor in the inner surface of the tube, but filters the ultraviolet emission of the gas by means of a Wood's filter transmitting only the radiation in the UVA range.
3. **Thermography** is a non-invasive and non-destructive analysis technique that relies on IR ( $8 - 14\mu m$ ) image acquisition. The use of thermography allows the reading of radiation emitted in the infrared band by bodies subjected to thermal stress. Radiant energy is a function of the surface temperature of materials, which in turn is conditioned by thermal conductivity and specific heat, which express in quantitative terms the ability of the material itself to transmit heat or retain it: a material with high values of conductivity will heat quickly and just as quickly cool. An IR thermographic system consists of a camera connected to an image processing and recording system. The IR detectors are responsible for detecting the consistency of the radiation that strikes them and for analyzing the radiating

surface point by point to arrive at the definition of the heat map. Recently this technique has been used in wound care in order to analyze the state of infection of inflammation of wounds, mostly on burns [26, 27].

## 2.2 Overview of Non-Optical Imaging Techniques in Wound Care

As mentioned in Section 2 there is a class of technologies that incorporate the non-optical imaging techniques. These, differently from the optical imaging devices (described in Section 2.1) do not measure the intensity of a transmitted, refracted or reflected light beam, but elaborate an image that comes from data gathered from the results of other chemical and physical phenomena. In last years many different techniques, technologies and devices that can be included in this field have been developed and brought to the market. Their main advantage is that by sensing physical phenomena and chemical reactions that are not associated to the emission of photons, these solutions render possible the elaboration of images given by a variety of different physiological factors that otherwise would not be able to analyze. In the field of wound care two of these are the most relevant since they are used in order to detect mostly inflammatory pathways and hemodynamics and these are the ultrasonography and the Magnetic Resonance Imaging (MRI).

1. **Ultrasonography** or more simply **ecodoppler** (or rarely **dopplersonography**) is a non-invasive therefore easily repeatable technique used in medicine to study the anatomical and functional status of blood vessels, arterial and venous, and the heart in real time and simultaneously (Duplex-Scanner). It takes its name from its physical principle of operation, the Doppler effect. Used for more than three decades, it has considerable value in both diagnostic, prognostic, and therapeutic fields in cardiac and vascular disorders which are one of the main causes of chronic wounds [28]. With the use of ultrasonography, through B-mode images, the morphology of the walls, their motility, the presence or absence of endoluminal formations, and the structure of the "atheromasic plaque" are studied, while with pulsed Doppler, the hemodynamic situation of the blood flow at that particular point is assessed through spectral analysis and the degree of purity of the sound, and thus the various degrees of stenosis can be quantified, distinguishing hemodynamically significant from non-hemodynamically significant stenoses. The morphological characteristics of atheromasic plaques can also be assessed, based on their echogenic features. This methodology is currently being supplemented with blood flow staining for even more precise information on blood flow. The exploitation of the Doppler effect in ultrasonography can have different characterizations, all used in the assessment of the vascular structure of the given body region. Amongst the most commonly used we can find:
  - a. **Color Doppler** is indicated for the study of vascular structures. In fact, thanks to the coloring performed by computer, the movement and direction of blood flow can be studied. The principle is based on the real-time association of a two-

dimensional ultrasound image with a pulsed Doppler signal. Conventionally, red color is attributed to structures approaching the probe, and blue for those receding. The method has revolutionized the diagnosis of vascular and cardiac diseases with the ability to detect and monitor arterial and venous stenosis, aneurysms, deep venous thrombosis, and chronic venous insufficiency over time.

- b. **Power Doppler** is similar to color-doppler, but it measures the frequency energy of the structures being examined. This gives a more sensitive signal but no information about the direction of motion of these structures. It is applied when a complex parietal lesion, such as an ulcerated plaque, is to be observed with greater color persistence, or it is used to better visualize the internal vasculature of an organ (liver, kidney, thyroid, spleen).
  - c. **Doppler Flowmetry** allows to analyze the flow pattern within vessels and thus highlight stenoses or closures.
2. **MRI** is an imaging technique used mainly for diagnostic purposes in the medical field, based on the physical principle of nuclear magnetic resonance. The adjective "nuclear" refers to the fact that the density signal in MRI is given by the atomic nucleus of the element being examined, whereas, in more widespread radiological imaging techniques, X-ray density is determined by the characteristics of the electronic orbitals of the atoms hit by X-rays. MRI is not harmful to the patient, and the patient is not subjected to ionizing radiation as in the case of techniques making use of X-rays or radioactive isotopes. The information given by MRI images is essentially of a different nature than that given by other imaging methods: in fact, discrimination between tissues on the basis of their biochemical composition is possible. The principle of operation is based on subjecting the patient to a strong static magnetic field. The magnetic field strength can range from tenths of a tesla, for small machines dedicated to the study of joints, and up to 3 T for machines currently on the market for diagnostic purposes. The importance of this examination lies in the fact that it is possible to discriminate, for example, between a liver tissue and a spleen tissue (which with respect to X-rays have the same transparency), or healthy tissues from lesions, given to the different relaxation times of the molecules of the different tissues when exiting the spin given by the magnetic field of the device.

### 3 Wound Measurement Techniques

"Good measurement derives from good sampling" and "You can't manage what you can't measure" are the two main aphorisms that are taught to students that enter the world of measurement, also known as *metrology*. Every expert in this field would state that both sayings are true. In wound care measurement is still an area where a dominant standardized model is not yet consensually accepted by its key opinion leaders. This is due to the facts that are described in Section 1: there are too

many variables to take into consideration in order to perform a precise assessment of a wound that range from its chemical to its morphological proprieties. There are some, though, that have to be taken into account. Historically speaking, wound assessment has always been performed primarily by the correct evaluation of its physical size through time. King Henry VIII Tudor of England (1491-1547) is also known for having suffered of a cutaneous ulcer at the right leg, that started after an injury during a hunting party. Nowadays, analyzing the historical evidence, we are able to state with certainty that his wound that seemed to be acute and traumatic has never healed since he suffered from Cushing's syndrome. In any case it is textually reported in the *Enciclopedia Britannica* [29] that "[...] *To soothe His Majesty's pains the most learned physicians in the World were called in. [...] Assessing the extent of the wounds, new bandages were applied, but without being able to heal him completely [...]*". Though the methods that were used at the time to cure the King were essentially bloodletting, wraps with soothing herbs and removal of necrotic tissue, it is clear that the most comprehensible variable for his surgeons was the wound size. Secondly, different studies [16, 17] that state that the morphology of the wound is at least one of the key indicators of good healing process. Moreover it is a fact that wound size measurement is one of the quickest and easiest ways to understand its clinical state, taking into account the means of imaging (data collection) described in Sections 2.1 and 2.2.

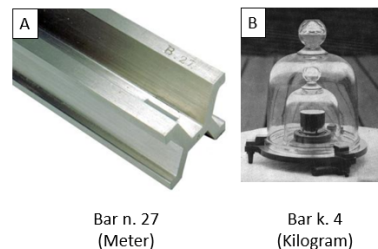
Taking into account the everyday good clinical practice, it is clear that the primary need of wound care specialists is to be equipped with tools that can help them to render a good, quick and precise wound assessment. Considering the features and capabilities of the technologies described in the previous sections of this chapter, the following discussion will be centered on the available techniques of wound measurement (i.e. optical imaging techniques) since it has been clinically proven that in this field are the most reliable, the most portable and the most integrable in the normal wound care clinical procedures.

Before parting with the description of the measurement means in the field of wound care, it is necessary to answer a fundamental question: *what does measurement mean?*. In the mathematical, physical and natural sciences, measurement is the assignment of a range of values (measure) to a particular physical property or chemical property called a measurand, defined through a physical or chemical quantity. Measurement is thus the process carried out to assign a measure, although in common parlance it is customary to use the term measure instead of measurand and presupposes the existence of a system of measurement. The term measurand does not refer to the object or phenomenon on which a measurement is being made, but to a specific quantity that characterizes them: for example, when we measure the temperature of a liquid, the measurand is not the liquid, but its temperature. Lord Kelvin, the famous physicist from which the International Standard gave the name to the universal unit of measurement of temperature, stated in 1883 "*When you can measure what you are speaking about and express it in numbers you know something about it; but when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind.*" Due to experimental and theoretical issues the measurand is not, in reality, describable by a single numerical value, even assuming

infinite measurement precision. Each measurement is thus defined as an interval of values within which it is likely to lie. The width of this range defines its precision: the larger the range, the lower the precision associated with the measurement. The development of metrology has led to definitions in statistical terms of the definition of measurands, and to the introduction of the concept of measurement uncertainty. The latter, to a first approximation, can be defined as the width of the range of values: the larger the range, the greater the measurement uncertainty. In the most common case, uncertainty is defined as the statistical distribution of a (virtually) infinite sample of measurements made on the measurand. The interval is associated with a numerical value identified with the mean of the measurements. Therefore, in metrology, a measurement is always defined with three components:

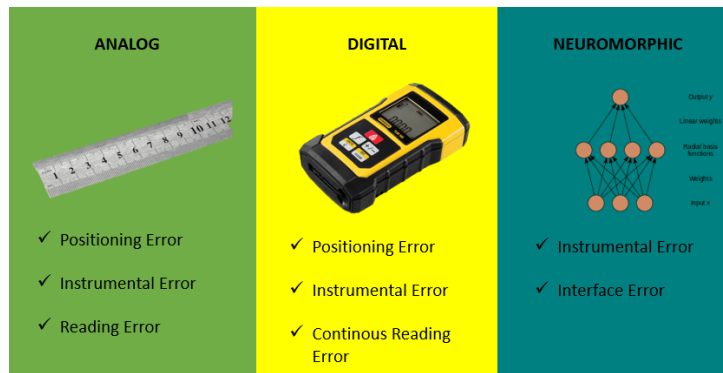
1. The numerical value;
2. The unit of measurement of the quantity, or the scale of the property;
3. The uncertainty associated with the measurement.

The study of measurement and of the understanding of standardized measurement system (i.e. metrology) is not new and it is possible to extract its arbors from ancient times. With the French Revolution came a turning point: the metric system was born. Various thrusts from the world at that time led the constituent assembly to adopt a new system based on the meter, that is, based on a natural magnitude, the 40,000,000th part of the earth's meridian. The platinum-iridium bar used as a sample of the meter from 1889 to 1960 (shown in Figure 4-A. From 1875 to 1889, the International Bureau of Weights and Measures made and distributed some 30 samples of the meter and kilogram. The metal chosen was an alloy of platinum with 10 percent iridium, refractory metals that had not yet been manipulated in such quantities and whose purity and homogeneity were required to be very high for the time. Since then the science of measurement, metrology, has made great strides, creating systems (including the SI) that have enriched and simplified the metric system, hand in hand with the evolution of science and technology. In other words measuring something parts, under a theoretic point of view, from the comparison of the measurand with a well known reference. In Figure 4 are shown both the *bar n. 27* and the *bar k. 4* that have served for reference of distance and weight measurements.



**Fig. 4** A - The bar n. 27 that served as reference of the meter from 1889 until 1960. B - The bar k. 4 that still serves as reference of the kilogram.

Centering the discussion on wound care, EDIs (see Section 2.1 for further explanation on these systems) exploit three different techniques of wound measurement

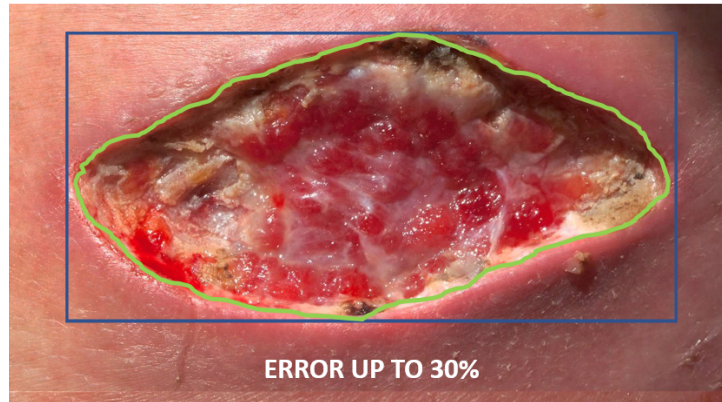


**Fig. 5** The three different kinds of measurement techniques implied in wound care. In the figure are reported the different kinds of errors that these method lead to and that have to be taken into account in a diagnostic decision. Although some errors might be the same for different techniques, their entity varies due to the technologies and the methodologies that are exploited when choosing one technique with respect to the other.

that are summarized hereafter and in Figure 5: analog, digital and the new *neuromorphic*. According to what has been just stated, each method implies one or more types of measurements errors. As in any other field of study, the best method to use is not only given by the absolute entity of the error, but also how the entity of the error effects the consequences of the measurement. In other words the wound care specialists should ask themselves: *"Is the measurement error of the method that I'm using leading to a clinically relevant outcome?"*

### 3.1 Analog and Digital Measurement Methods

The difference between analog and digital techniques of measurement basically resides on who is actually performing the comparison between the measurand and the measurement reference. Analog measurement implies a direct comparison between the two and this is performed directly by the operator, one example can be the measurement of a line with the use of a ruler. In digital measurement the comparison is performed by a dedicated device that acquires the information of the measurand and through fixed mathematical rules returns a number that should be equal to the entity that is to be measured. In the last ten years the first EDIs hit the market and have been tested in standard clinical procedures regarding wound assessment and monitoring. These devices present different functionalities and perform measurements exploiting different techniques. The one thing in common is that they have all been designed to (also) perform morphological measurements of the wound. In some cases these measurements are only bi-dimensional, in other cases the solutions are able to measure the wound's depth and volume. Though these techniques are becoming



**Fig. 6** In figure is shown a generic wound framed inside a rectangle. Due to the irregularity of the wound's shape, the area of the rectangle and the area of the wound can have up to a 30% difference.

more and more popular, there is still a large number of specialists the uses analog measurement techniques that in some cases present a high degree of empiricity.

Analog measurements in wound care were and are still usually performed with simple rulers for the calculation of the wound surface, and with cotton swabs inserted in the wound bed in order to obtain a rough evaluation of the lesion's depth. This technique presents several problems. First of all it can be painful for the patient: the insertion of an object inside the wound bed or the simple touch of a ruler with the damaged skin can cause a high degree of discomfort. In this case different discomfort are felt both the patient and the operator, since the later has to perform an objective measurement while the patient is moving in pain consequently increasing the degree of approximation of the measurement. Secondly, when measurements are taken by hand, the returned values have to be transferred in a clinical folder or a report that can be on paper or digital, increasing bot the time consumption of the visit and the risk of losing the acquired data. Lastly wounds have an irregular shape and its size is very difficult to calculate by hand without the aid of a computational mean, especially if it is measured with a linear ruler. Many operators try to go around the problem by "framing" the wound inside a regular shape such as a rectangle or a square, and take the the surface of the encircling shape as the wound's area. This incorrect approximation error can lead to measurement inconsistencies that can be up to 30% as shown in the example in Figure 6.

Digital measurements in wound care are usually performed though EDIs that are devices that in the majority of the cases implement a CMOS camera in order to take the picture of the lesion and distance sensors (see Section 2.1 for further details on these devices). By taking a picture of the wound through the digital camera, the image is automatically discretized in a number of regular pixels given by the camera's intrinsic resolution (the resolution depends on the camera's sensor). By reading the distance of the camera from the plane on which the wound lays through the distance sensors it is easy to understand the size of the physical area depicted by

each pixel in the picture. The operator then, through the device's screen or through other methods of interaction with the device, digitally traces the wound's perimeter and the EDI easily calculates the wound's surface. In some cases the EDIs do not have distance sensors that can read the distance between the device and the wound and so other techniques are implied in order to have a correct match between the pixel and the size of the area that they depict. One simple technique that is used by different producers is the so-called *blue dot technique*. This procedure implies that the operator lays a physical reference (usually a sticker) that has a known color, size and shape in the field of the image. The picture is taken with the device that recognizes the sticker thanks to its color and automatically calculates the number of pixels in the resulting image that show it. Since the EDI has in its memory the actual size of the sticker it can easily calculate the depicted area by each element. The rest of the procedure is the same as in the other EDIs: after tracing the actual contour of the wound in the image the device counts the pixels and easily arrives to calculate its surface. There are different devices in the market that have been widely clinically validated which use the blue dot technique. The most common and well known is the Moleculight™ and its clinical study is reported in the work by Kleitjes *et al.* The blue dot technique offers also the possibility to implement measuring functionalities to devices without the use of added sensors (a part from the CMOS camera): this implies the development of mobile applications that can be installed on personal devices such as smartphones and tablets. One of the latest is represented by Imito™, an all-around smartphone application for ulcer management [30]. Imito, in particular, uses its token also as a color reference in order to easily discretize the tissues composing the analyzed wound bed.

EDIs that perform a digital measurement of the wound have several advantages over the analog methods. First of all the measurements are for sure more precise due to the possibility by the operator to easily calculate an irregular shape like the ones of wounds. Secondly EDIs are non-invasive devices, for this reason the patient's experience and quality of life during the assessments increases sensibly. In many cases though both methods of measurement present several errors that can be due both by the operator and by the intrinsic characteristics of the devices as reported in Figure 5. The same errors are briefly explained hereafter and in Table 1 are reported the mean entities of each measurement error for each measurement technique.

1. **Positioning error:** this inconsistency occurs when the measurement device is not physically placed correctly on the measurand. This might happen when using a ruler and the reference tick does not coincide precisely with one of the ends of a wound. When using an EDI this might occur when the picture of the wound is not taken precisely parallel to the wound's plane.
2. **Instrumental error:** no measuring device is 100% precise. There always are some inconsistencies between the real physical entity and the device's actual scaling. Usually the entity of this error is reported by the producer, and in case of the EDIs is very low. In EDIs this error is usually negligible.
3. **Reading error:** this kind of error strongly depends on the operator when using an analog measurement technique. Even if the ruler is precisely placed with respect to the measurand, the reading can be subject to the position of the operator with

**Table 1** Comparison of the error entities with respect to the measurement techniques. These values have been calculated on average size wounds (between  $1\text{cm}^2$  and  $10\text{cm}^2$ ). The values reported on the table are the maximum expected errors on the total measurement.

Measurement Technique	Positioning Error	Instrumental Error	(Continuous) Reading Error
Analog Mes.	up to 20%	up to 10%	up to 50%
Digital Meas.	up to 10%	up to 1%	up to 5%

respect to the ruler when performing the measurement. To help understanding this phenomenon it is necessary to think of the reference tick of the same ruler. Each tick reports a distance from its previous one and the one after, but also the ticks have their own dimension such as a width. Depending on the initial reference is taken from the beginning of the tick or its end the measure can change. This error is higher when the measurand has a dimension similar to the basic scaling of the ruler (i.e. when measuring entities that are less than one centimeter when using a normal linear ruler).

4. **Continuous reading error:** this kind of error refers to only digital measurement techniques. As mentioned before a CMOS camera discretizes an image in a regular grid of pixels, and in an EDI the operator must trace the perimeter of the wound on a screen. The tip of the operator finger, or the cursor of a mouse or the tip of a pen usually have a size that is larger than the single pixel, and for this reason some inconsistencies in the total measurement can occur. As for the reading error in analog techniques, this error decreases exponentially with the increase of the total size of the measurand.

### 3.2 Neuromorphic Solutions in Wound Care

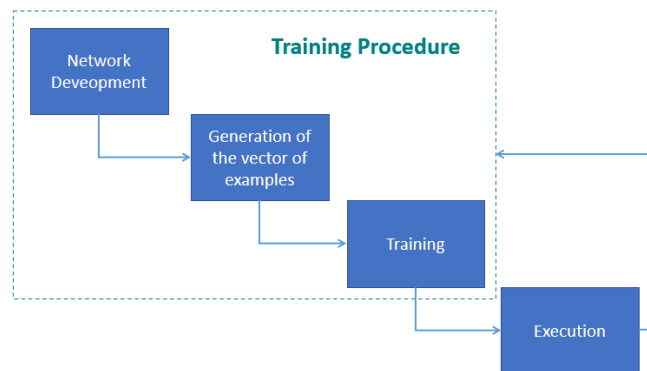
In the last few years this new class of EDIs has proven its efficacy in the field of wound care for their high precision of measurement and of classification. *Neuromorphic* EDIs differ from the rest of the devices since they implement artificial intelligence algorithms that are able to analyze clinical images and automatically identify and classify the wound with respect to several clinical classification scores.

Neuromorphic engineering (also called neuromorphic computing) is a concept that started at the beginning of the nineteen-seventies that had the scope to develop systems, both software and hardware, able to analyze large amounts of data mimicking the biological-neural architectures of the brain [31]. One of its branches is devoted to developing what are known as Artificial Intelligence (AI) algorithms that are computational methods able to solve complex problems with large amounts of data. In the years, many different types of AI algorithms have been developed and used in different fields, but amongst the most commonly used we can find the Artificial Neural Networks (ANNs) and its derivatives. ANNs are the computational struc-

tures that have to be designed in order to solve a given problem (i.e. classification, statistical inference, etc). Their particular structure implements two basic elements that can be arranged accordingly to the given problem that has to be solved:

1. **Nodes:** these are the basic computational structures of the network and symbolize the input, transfer and output data. They should work as biological neurons.
2. **Links:** the links, as the name suggests represent the mathematical relations between two or more nodes. These elements simulate biological synapse.

As in the biological brain ANNs do not change their initial structure, but change the values associated with the different links and nodes that work as mathematical operators with which the input data is treated. Indeed ANNs, and in general AI algorithms, vary from normal computational routines due to their evolution dynamics. In other words, while in classic informatics algorithms are coded in order to perform a pre-determined sequence of actions on the data, AI algorithms are instead *trained*. Training a network means presenting an input set of data and the elements of its structure change their internal values in order to treat the data according to the problem that has to be solved, this phenomenon is also known as Machine Learning (ML). An example of a general training process of an AI algorithm is represented in Figure 7. Training the network, under an operational point of view, means extracting the *features* from the data that has to be analyzed. These features can vary, but in general they can be described as the characteristics that unite different groups of data for classification and correlation purposes.



**Fig. 7** The figure shows a "normal" training procedure of an AI algorithm. At first the network is designed and coded. Then a vector of examples (i.e. a group of initial data) is presented to the network as input. Then the network evolves: its nodes and its links change their internal values in order to sort and analyze the data as required by the developer. Afterwards there is Execution of the algorithm, where its computational efficiency is tested. If the results from the execution do not meet the required standards, other training sessions are performed until the optimal efficiency is reached.

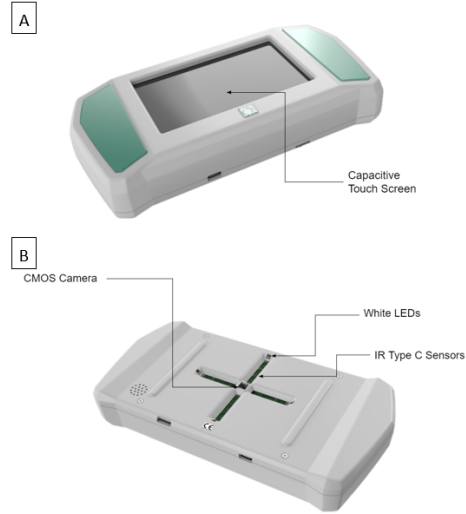
Due to their intrinsic properties, neuromorphic EDIs present several advantages with respect to the classic devices. First of all, measurement errors that are due to

human factor are depleted: neuromorphic EDIs, if well trained, are able to analyze images and distinguish automatically the desired objects. For this reason the segmentation of wounds in the images taken by the device reaches the highest precision possible. Moreover these devices are able to perform other analysis on the data, for instance, as they are capable to distinguish and segment a wound, they are also able to distinguish the different tissues that compose the wound bed, and so able to perform a clinical classification of the lesion with respect to validated standards such as the WBP score. As all means of measurement though, these devices are still affected by two types of measurement errors:

1. *Instrumental error*: these device suffer as all other EDIs suffer from the instrumental errors given by the measurement components that they implement (for example any distance sensor that is used to dimension the pixels that depict the wound through the distance of the device from the lesion's plane).
2. *Interface error*: This error occurs during the training procedure of the algorithm. Its computational efficiency (i.e. its actual capability to correctly analyze the data, such as an image) is given by the quality and the amount of data used for the training of its algorithms. If in such data there are mistakes, or it is lacking of intrinsic information, the algorithm will erroneously learn the mistake or be imprecise in its outputs.

One of the newest devices that has been recently clinically validated and is entering the good clinical practice in wound assessment is the Wound Viewer (WV), developed by Omnidermal Biomedics (Italy) [32]. The WV is a skin wound assessment tool designed to measure and collect data regarding patients and their wounds. The device is non-invasive, does not come into contact with applied and accessible parts and can be used for both ward and home visits. The device and the related software is to be considered as an adjunct tool for wound care management that is not intended for diagnostic purposes. This device was designed to run the proprietary artificial intelligence algorithm for wound measurement and assessment. The device is equipped with a 5MP colour CMOS camera sensor to acquire high resolution pictures, 16 high precision IR distance sensors and 4 white LEDs. Users are supposed to control the device through a dedicated front end through a capacitive touch screen display (Figure 8).

The ulcer analysis algorithm implemented in WV applies a Discrete Time Cellular Nonlinear Network (DT-CNN) computing architecture in order to identify the wound hence providing relevant measurements of its area, depth and volume [33–35]. Those acquired measurements include the wound area expressed in squared-centimeters, the wound depth expressed in millimeters and the wound granulation expressed through the WBP score. DT-CNN is a parallel computing paradigm, introduced by Chua and Itoh [36], similar to artificial neural networks for processing any-dimensional signals. As any other bio-inspired neuromorphic algorithm, the DT-CNN goes through a learning phase and an inference phase. The cellular nonlinear network in the WV algorithm, which processes a 2-dimensional colour image, in the former phase is provided with statistical information about the tissue forming the wound bed through a colour analysis. Those statistics are extracted from the training



**Fig. 8** The WV device shown in its A - top and B - bottom view. The figure highlights its main elements such as the type-C IR sensor, the CMOS camera, the white LEDs and the capacitive touch screen.

set by a digital segmentation of wound areas in the images contained in the training set (more than 1500 wound pictures). The resulting statistical information takes the form of a mapping, hereafter named  $g(\bullet)$ , or in other words an  $\mathbb{R}^3$  function, between each of the 16,777,216 possible 24bit in the RGB color space [23].

The nonlinear processing units making up DT-CNNs are often referred to as neurons or cells. Those cells can be implemented, depending on the underlying technology, as arbitrary independently computing units, this results in a very fast parallel algorithm to run. When using a DT-CNN to perform an analysis of an image, like in the case of the WV algorithm, each cell of the DC-CNN corresponds to a pixel of the digital picture. Under a mathematical point of view  $I$  be the 2-dimensional RGB colour image and  $O$  the computed black and white image underlying the wound area (both having dimensions  $W \times H$ ,  $\Theta(\bullet)$  be the Heaviside function and  $N$  an even integer number. By appropriately setting the parameters  $\theta$  and  $\rho$ , which are the cell's and the automata threshold levels respectively, the image  $O$  can be computed by applying the formula in Equation 1 where  $(i, j)$  are the coordinates of a single pixel and  $I_{i,j}$  is the pixel RGB triplet code while  $O_{i,j}$  is the pixel of the binary output image:

$$O_{i,j} = \Theta\left(\sum_{h=1}^{i+\frac{N}{2}} \sum_{w=1}^{j+\frac{N}{2}} \Theta(g(I_{i,j}) - \theta) - \rho\right), \quad (1)$$

where

$$\begin{cases} 0 \leq i \leq H - 1 \\ 0 \leq j \leq W - 1. \end{cases}$$

As an example, the elaboration result of the wound in Figure 9. The original image in (Figure 9-A) went firstly through a pre-processing phase and then presented to the trained DT-CNN. Each automata part of the network, using the statistical chromatic

knowledge stored in  $g(\bullet)$ . Then the output  $O_{i,j}$  was computed by counting the number of pixels in a given proximity ( $N + 1$ ) of the input element  $I_{i,j}$  whose colour appeared enough times (more than  $\theta$ ) in the wounds from the training set. The total number of pixels verified to be characteristic of a wound area are then compared to the threshold level  $\rho$ . If this critical value is lower than the weighted counted number of pixels then the pixel  $O_{i,j}$  is reported to be part of a wound area (set to binary true, white in (Figure 9-B)), else it is rejected.



**Fig. 9** A - Example of a wound image before being analyzed by the WV device's algorithm. B - Resulting binary image where it is possible to note that the edges of the wound coincide with the borders of the binary mask given by the discrete time-cellular nonlinear network (DT-CNN)

Regarding the wound classification, the algorithm takes solely into account the pixels that were recognized as part of the wound (i.e. white elements in Figure 9-B). Once the whole surface of the wound is recognized, the highlighted elements are analysed regarding their colour scheme (RGB). The whole set of possibilities regarding the colour of pixels forming the wound has been classified in four macro groups: red, white, black and yellow. The wound images in the training set have been classified through the WBP score (in granulation) and then matched taking into account the presence of the four macro groups in the wound area. Through this training phase the algorithm is able to analyse these colour schemes and perform an automatic classification.

### 3.3 Clinical and Economical Advantages Resulting From the Use of Neuromorphic EDIs

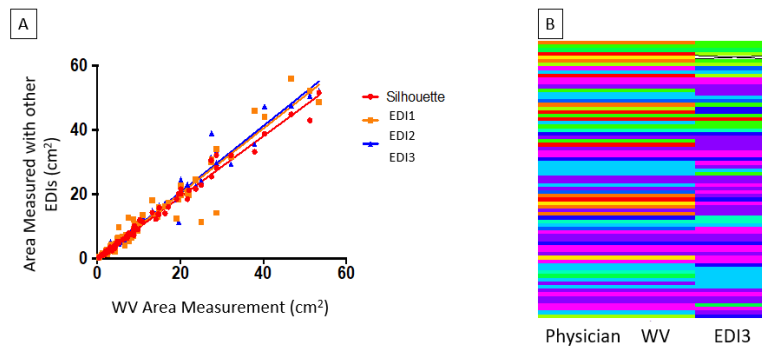
In Section 3.3 neuromorphic EDIs have been described with respect to the previous generation of the same device class, describing its advantages in terms of measurement precision and classification capabilities. In particular the WV device has been taken as an example for two reasons: first to provide a better understanding of the analysis that these kind of devices perform in a wound assessment session, second because it underwent a clinical trial that proved its measurement efficiency as well as its ability to be integrated in the common good clinical practice described in [23].

The study rationale parted from the fact that skin ulcers are treated with continuous and periodic dressings that are carried out by the specialist in charge. During a normal assessment, the wound care specialist manually or with the help of an EDI, measures the extent of the wound and applies a new dressing. As mentioned in Section 3 one of the main characteristics that are taken into account are the differences of the morphology of the lesion between two different assessments. Another variable that is usually taken into account is the wound bed and its composition and a classification through a standard clinical scale (as the WBP) is performed. The standard EDIs can result in being time consuming and less intuitive since there is no process of automatic analysis of the wound, on top of the fact that the operator actively participates in the wound measurement increasing the risk of errors. The purpose of the trial was therefore to verify the ease of use of WV in a normal wound assessment session, comparing its results with the other three EDIs. Regarding the wound bed, its correct classification is taken into account as a critical variable since it can be taken as a guide for therapeutic decisions. Before neuromorphic EDIs, such as WV, wound classification was at the only prerogative of the specialists, and depending on the degree of its clinical experience this can result in being subjective and difficult to standardize. WV and this class of devices aim to overcome the subjectivity inherent in the system through automatic evaluation through its AI algorithms. In details, the aim of the trial was to verify that the WV is able to automatically identify the wound in the image and perform a correct measurement and classification of the lesion, suitable for providing high standards of cure.

The clinical trial, has been performed at the Department of General Surgery at the Azienda Ospedaliera Universitaria San Luigi Gonzaga (Orbassano, Italy - protocol number OC15194). It has been conducted on 150 patients divided into three cohorts of 50 patients each according to the type of wound: lower limb ulcer, diabetic foot ulcer and pressure ulcer. Once the patients were enrolled in the study and gave their informed consent to participate in the trial, their wound were measured with WV and with other three classic EDIs, whose measurement capabilities are universally known as precise. At the same time the operator classified the wound through the WBP score in granulation, then compared its classification with the one returned automatically with WV and the one that resulted from the classification of the wound bed tissues made by one of the other three EDIs.

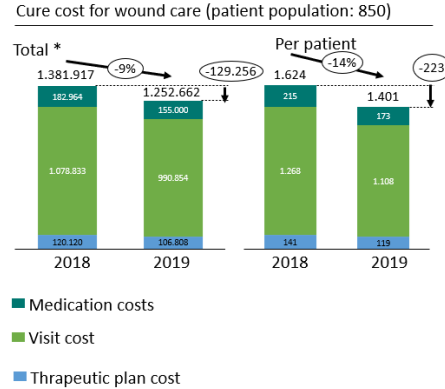
The measurement distribution of the patient population was compared through inferential statistical analysis in order to verify the similarity of the results obtained from all the devices used in the trial. Through a Kruskal-Wallis one-way ANOVA analysis a  $p\text{-value} = 0.9$  proving that the distributions were in fact the same and therefore the automatic measurements of the WV could be considered precise (Figure 10-A). In addition in all the cases the WV device was able to correctly according to the visual assessment of the physician performing the assessment, differently from the compared EDI whose classification capability proved to be unsatisfactory for clinical standards (Figure 10-B).

The WV has proven in the years to be effectively integrable in the everyday clinical practice, not only in wards, but also in telemedicine procedures. In many places of the world, and most importantly, after the COVID-19 pandemic, the capability to



**Fig. 10** A - Distribution and comparison of the morphological measurements performed by WV with respect to the other EDIs. B - Comparison of the wound classifications (using the WBP in granulation) performed by the WV with ones performed by the physician and the employed EDI for this particular scope.

monitor a patient while at home instead of hospitalizing him has become more and more crucial. Telemedicine in wound care though presents different issues. First of all the care givers (i.e. physicians and nurses) that treat the single patient may vary over time leading to inconsistencies in the therapeutic plans, in the prescriptions and in the clinical assessments. These inconsistencies, a part from the fact that they can worsen the quality of life of the patients, consequently lead to a reduction of the cost-effectiveness of the various cures. The lack of a standardized mean of wound assessment and the incapability of the hospitals to centrally monitor the situation of their patients has become one of the major pains. In a hospital in Italy, the WV was uptaken for this specific reason and the data regarding the cost of cures between the year before the use of the technology and the following were compared (Figure 11). It must be noted that the total cost is divided into three major expenditures that are: the medication costs (i.e. the cost of the prescribed dressings, the visit costs (i.e. the cost of the single specialist traveling through the territory to perform a medication) and the cost for the therapeutic plan (i.e. the administrative costs for medical prescription). Surprisingly, thanks to the use of WV and its capability transmit the information amongst the operators directly into the patient's Electronic Medical Record (EMR), the wound care specialists were able to administer the right therapy to the single patients according to their general clinical state. Moreover it was possible to render efficient the general operations regarding the patient management, concentrating the operators on the patients that required greater treatment and attention, lowering the number of visits to the ones that were going through a correct healing process. From these logical actions taken by the hospital through the use of his neuromorphic EDI, the total cost reduction for the hospital (on a population of around 850 patients per year) has reduced by 9%, while the cost of cure per single patient reduced by 14%.



**Fig. 11** Reduction of the cost of cure (total and per single patient) in telemedical procedures regarding patients with chronic wounds. The values reported in the Figure are in Euros [€].

## 4 Conclusions

Telemedicine is currently at the forefront of integrative technology with the goal of improving clinical care while reducing costs in all medical fields, such as wound care. In this chapter an *excursus* of the most employed technologies in wound care has been presented and described. Many of the devices and techniques that have been reported were not available until ten years, others even less. These last years, under a technological development point of view, have proven to be the most interesting in this field thanks to the effort of many researchers, clinicians and companies that work with the sole goal to provide devices for accurate wound assessment. But the work is not yet done: many more advancements in the field of imaging and measurement in wound care will come in the future years. This is mostly due to the fact the COVID-19 pandemic has shown the world that these kind of devices can have a great positive impact in clinical practice. The last class of devices presented are the neuromorphic EDIs: these represent the most recent advancement in this particular field, and with the example given by the WV device, their efficacy is clearly proven.

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