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context

Smart textiles for healthcare and medicine applications (WG1)

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ABSTRACT

The aim of this document is to provide information on the state-of-the-art related to the topics covered by each working group within the CONTEXT project. It provides information on materials and technologies used to develop smart textiles with targeted performance, general applications of smart textiles in the field, case-studies on the use of smart textiles, opportunities for smart textiles considering the needs of each field, trends on the development of smart textiles in terms of market and technical expectations.

This paper gives an overview of the potential of smart textiles for healthcare & medicine, ongoing developments, state-of-the-art products and future developments.

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1. INTRODUCTION

There are remarkable improvements and new potentials in the textile field over the last few years thanks to the integration of smart materials and electronics. These new textiles are called "smart textiles" and smart textiles can be defined as textiles that are able to sense and respond to changes in their environment.[1] Significant progress has been done in smart textiles in parallel to the improvements in the microelectronics, artificial intelligence and new lifestyle of the population. Lately, there is an increasing trend of integrating intelligence in our daily environment. These novelties brought innovative high-tech applications and new market segments to the conventional textile. Also, that gathered specialists from different field and created an interdisciplinary technology. The smart textile market is a niche of the future that is in full development with unique applications for different use cases. Smart textiles find many applications in different fields. In particular, the projects in healthcare, military and defense, sports and fitness, automotive, entertainment, and personal protective equipment field, respond a real need. Today, these applications allow us to avoid many accidents, diagnose earlier, treat certain conditions in a more effective way and, potentially, extend life expectancy for the end-users.

Smart textiles have the potential to face numerous health and well-being challenges, such as diabetes, obesity, mental health, neurodegenerative diseases, cardiovascular diseases, stroke, cancer, motor rehabilitation and for regeneration of organs.

The development of smart textiles in this field requires to solve specific technical and regulatory challenges: reliability and consistency is essential with health-related data, with the fabrics having to withstand harsh conditions such as body swear, wash cycles, and temperature variances while still functioning effectively, ease-of-use and wearability are also important aspects, as well as the need to meet clinical regulations in the process.

In this paper, the innovative applications of smart textiles in the medical and healthcare field will be discussed, with their market adoption driven by their exciting and promising future potential regarding health monitoring and activity tracking.

2. SMART TEXTILES FOR HEALTHCARE AND MEDICINE APPLICATIONS

2. 1 Smart textiles for monitoring and sensing

Currently, the world's population is expected to rapidly increase and reach 9.9 billion by 2050 (according to the Population Reference Bureau). The shift in global demographics shows that the population is aging due to a decline in mortality rates. As a result of the growing geriatric population, as well as the increasing incidence of chronic lifestyle diseases, Western countries are addressing high costs for medical and long-term care needs. Those market drivers are pushing the interest in smart textiles for remote monitoring and sensing.

There are already wearable products on the market which were used to monitor activity and the wearer's health arameters such as pulse rate or oxygen rate; however, smart textiles may transform the monitoring and the collection of these data, guaranteeing more accurate and realistic results while preserving the comfort, thus re-defining their potential impact on healthcare.

2. 1. 1 Smart textiles for monitoring and sensing obtained by integrating electronics

Several studies investigated the utilization of e-textiles for health scenarios. These innovations may revolutionize the way in which medical practitioners operate. These textiles require digital components and embedded batteries to work. Generally, for this type of applications, the utilization of conductive fibers or inks is very common with the traditional textile processes such as knitting, weaving, printing etc. Reliability, performance consistency over time, and comfort are the most important points to guarantee their adoption. Some examples of smart textiles products or projects are described below.

Rhode Island University Biomedical Engineering Department has done researches on quantitative measurement of akinesia in Parkinson's disease. This disease is a motor disorder which affects upper and lower limbs, limiting movements ability with frequent tremors.[2]

Researchers developed a smart glove (fabricated with a neoprene textile with circuits made from conductive thread, including a flex sensor to detect the range of motion, an inertial sensor to detect tremors, and Bluetooth module for data transmission) to monitor Parkinsonians.[3, 4] These smart gloves give the possibility to determine the degree of mobility and potentially optimize the efficiency of prescription medication.

Two smart wearable projects were realized by Bioserenity for the monitoring of sleep disorders and neurology: Somnonaute and Neuronaute. The mission of the company is to provide continuous care to patients and health professionals with the acquisition and interpretation of electrophysiological examinations, such as EEG (electroencephalogram), ECG (electrocardiogram) and PSG (polysomnography).[5] For this aim, the company has collaborated with IFTH (French Institute of Textile and Clothing) to develop a wearable system with the integration of conductive flexible textile circuits and sensors.[6]

These sensors are positioned to obtain the required biosignals continuously to diagnose, analyze and give the posology adapted to the patient. Again, one of the benefits of this development is conserving the comfort of traditional textiles cloths, which improves the quality of the collected data.

Figure 1 - Bioserenity - Ambulatory mobile solutions for the diagnosis and monitoring of patients

A similar technology called "Hitoe" is developed by Toray for daily use.[7] Hitoe is not a medical device but it gives the possibility to collect bioelectric information continuously thanks to a highly conductive knitted polyester nanofiber fabric impregnated with a conductive polymer (PEDOT: PSS).[8] The heart pulse is sensed by the potential difference on each pulse of human heart. Hitoe functional material is washable thanks to Toray's advanced processing technology for high impregnation and the utilization of nanofibers which make the fabric resistant to washing cycles and obtain a high contact with the skin.[9]

In another project supported by the Swiss Innovation Agency, the goal was to develop a textile low impedance ECG electrode with optimized electronics for heat stress monitoring for fire fighters. For this, an Ag/Ti-coated PET yarn was developed to embroider textile electrodes. The electrodes showed a low electrical resistance of <10 Ω and good skin contact with low skin irritations, particularly as an integrated electrode humidification system was applied. The electrodes were integrated into a semi-elastic polyester belt for the application on the wearer's chest.[10]

Figure 2 - Hitoe™ bio-electrode conductive nanofiber fabric

Besides applications for occupational safety, the clinical applicability for overnight monitoring was assessed in order to screen patients for breathing related disorders during sleep. When compared to reference gel electrodes, ECG belt data showed acceptable quality (with regard to Signal-to-Noise ratio, SNR) and accuracy (standard error of estimate of 0.4%, Pearson r of 0.91). Therefore, it was concluded that the ECG belt is an applicable tool for continuous ECG patient monitoring.[11]

Likewise, Nuubo[12] is a wearable medical technology company which offers e-textile technology BlendFix sensor electrodes, for remote ECG monitoring with a cost-effective, simple, transparent and non-intrusive method.

Figure 3 - NUUBO wearable ECG unit

HealthWatch[13] is another company pioneer in harnessing e-textile technology to produce fashionable, seamless knitting, smart-digital garments with interwoven sensors unobtrusively measuring vital signs of hospital-grade quality. The company's first product is a sensor-rich heart sensing textile garment incorporating 12-lead ECG with heart rate detection, skin temperature, respiratory, and body posture, allowing ECG and wider vital signs monitoring, compatible with gold standard ECG monitoring.

Moreover, there are also some examples of connected maternity clothes. A bally band is knitted with conductive fibers to monitor uterine activity and assess fetal well-being.[14] The technology permits to collect biosignal from the infants and send them thanks to the RFID tag and a knitted antenna designed also by Drexel University.[15]

Smart socks are also a highlight product in smart textiles. Texisense in collaboration with IFTH has developed smart socks to reduce fall events for patients at risk. These knitted socks with conductive and piezoresistive fibers are designed for daily use and provide the same comfort of regular socks. Furthermore, these smart socks[16] may help prevent diabetic foot ulcers by alerting the wearer when there is so much pressure due to bad posture or bad-fitting shoes, as diabetic patients have reduced nerve functioning. Siren e-socks are also in the market for preventing foot ulceration by monitoring continuously the foot temperature. The monitoring system sends the collected information to the health professional, to help tracking the possible inflammations.

Figure 4 - Texisense e-socks (on the left) and siren e-socks (on the right)

Likewise, Sensoria partnered with the Michael J. Fox Foundation and Neuroscience Research Australia to launch a clinical trial for investigating how Sensoria smart textiles socks can improve care for Parkinson's disease by collecting data and by testing a haptic feedback that can prevent "freezing of gait" events in patients.[17, 18]

Figure 5 - Sensoriae-socks

Optical fibers have also many advantages for the utilization in wearable systems. They are light-weight, insensitive to electromagnetic fields, not releasing heat and they resist to water and corrosion.[19] Examples of luminous textile applications have been realized within the TecinTex and ParaTex projects.[20] In these projects, soft, ductile, skin-friendly POFs were developed by melt-spinning technology. Due to their ductility and small, yarn-like diameter, the melt-spun POFs were successfully integrated into textiles for sensing and therapy applications. For that purpose, the project team used both embroidery, as well as weaving and stitching. POFs incorporated into textiles have then been used to sense a range of metabolic parameters such as heart rate, arterial blood oxygenation, breathing rate, and pressure.[21, 22] The friction of these textile sensors against artificial skin models was lower than that of conventional medical bed-sheet, demonstrating a high level of comfort to the end-user; another important factor was breathability, which was proven to be similar to conventional, cotton-based textiles. In initial (nonclinical) trials with healthy subjects, such photonic textile sensors were shown to be equivalent to their medical counterparts such as pulse oximeters[23] and breathing rate detectors.[24]

Leal-Junior et al.[25] present a polymer optical fiber-based sensor as smart textile for the detection of strength of deformation monitoring. It is sited in the chest and study the deformation of the material to monitor the respiration. The system allows the detection of the breathing rate and gait cadence. Furthermore, the textile is combined with an oximetry to complement the information collected by the sensing system.

A similar example was reported by Jeong et al.[26] They have developed a fiber-based strain sensor for the monitoring of the angular movements of the elbow and the knee. It was prepared by combination of polyurethane, tin oxide and carbon nanotubes. The sensor is able to operate stably without influence of water or the body sweat. The distance between carbon nanotubes is dependent of the degree of stretching and tin oxide prevents the entrance of the water to the fiber.

One of issues related with smart materials for monitoring and sensing is biosensors development. Biosensors are small devices able to transform chemical information into useful analytical signal.

A typical electrochemical biosensor involves three main parts: (I) working electrode, (II) reference electrode and (III) counter electrode. The choice of the material for working electrode preparation has to be chemically inert, highly conductive, biocompatible, easy to modification and mechanically stable. Some of the alternatives are novel nanomaterials i.e. carbon nanomaterials (carbon nanotubes, graphene), noble metal nanomaterials (nanoparticles) as well as hybrid nanomaterials. The key component of the biosensors are reference electrodes with known potential.[27] The bio-recognition layer of biosensors can be received by bio-molecules immobilization via adsorption, covalent bond creation, entrapment or encapsulation.

However, these methods are time-consuming and, in many cases, need long-hours conditioning of solid support in bio-molecule solution. Therefore, there was a need development new, significantly shorter methods. One of the these is application of low energy Corona Discharges of plasma with close to room temperature generated under atmospheric pressure.[28]

The authors reported that during deposition of bio-recognition layers, enzymes molecules are polymerized/cross-linked inside plasma reaction zone and deposited onto bare electrode. In the work of Malinowski, Sz. et al.,[29] the plasma technique was utilized for laccase-based biosensors construction. As a result, the comparison of the biosensors constructed by plasma technique with conventional ones obtained by wet methods showed that Corona Discharge application allowed obtaining biosensors in significantly shorter time without losing their analytical parameters i.e. linearity or sensitivity.

BIOTEX, standing for Bio-sensing Textile for Health Management, is a European project of 6th Framework Program, which aims at developing wearable biochemical sensing techniques.[30] In the frame of this project, a sweat rate sensor has been developed for real-time measurements. The need of this product comes from the health issues which can be a consequence of dehydration.

It was observed on athletics that dehydration may influence their performance and cause serious health issues but also re-hydration excessive dose after exercise may cause many health issues like headache, nausea or brain damage.[31] Thus, a wearable sweat sensor has a great potential in sports and medical field.

In this innovation, the sweat is guided using a textile membrane based on polyamide lycra® blend because of its moisture wicking properties. Then, a passive pumping mechanism is designed for sweat and this channel is screen printed on the both sides of the fabric with an acrylic hydrophobic paste to transport the sweat to sensors.[32]

The innovation consists of two textile electrodes which behaves like 2 plates of capacitor, located in different heights on the skin. Thus, with the penetration of the liquid between the capacitors, the capacitance changes, making possible to monitor the sweat rate.

In 2018, KOB[33] established a Smart Medical Textiles Team, which is working on the integration of sensory solutions in bandages and fabrics with customers and research projects in international partnerships. Two of the main projects are:

ULIMPIA[34]

In the ULIMPIA project, sensor yarns are integrated into a textile carrier material. When processed into a plaster, they can record the temperature, pH and moisture of a wound and transmit them wirelessly. The continuous sensor-based wound monitoring can give an early indication of potential complications, particularly with chronic wounds.

Figure 6 - Ulimpia bandage

THERAFOLG-KOMP[35]

The objective of the THERAFOLG-KOMP project is to develop a system that uses textile sensors to enable the success of compression therapy to be measured and to make the results visible and useful for patients, doctors and manufacturers of medical devices. Acceptance of treatment should be improved by digital feedback of the success of the therapy.

→ Bio- Radar[36, 37]

The Bio-Radar is a non-contact system to measure vital signs accurately, such as respiratory and cardiac signal. For now, the prototype is focused on the respiratory signal exclusively. This system is based on the Doppler effect principle, that relates the received signal properties with the distance change between the radar antennas and the person's chest-wall. The received signal will be a phased modulated version of the transmitted signal, which occurs due to the chest-wall motion while the patient is breathing. This motion changes the travelled distance of the electromagnetic waves causing the phase modulation. The prototype is composed by a Continuous-Wave radar, performed by a Software Defined Radio operating with a 5.8 GHz carrier, two textile antennas for transmission and reception respectively, and a LabVIEW interface, where the digital processing algorithm is applied to extract the respiratory signal. This system has a wide range of applications, such as the continuous monitoring of critical patients, the control of patients with sleeping disorders, or even on safe drive in a car for example. Thus, it can be included in different environments, by customizing and designing textile antennas.

2. 1. 2 Smart textiles for monitoring and sensing without electronics

Chromic materials have an application area in smart textiles without electronics. These materials can change their color according to external conditions and may utilized for functional purposes.[38] Different kinds of chromism are named after the stimuli that cause color changes.[39]

The external stimuli "X" can be varied in the presence of an intelligent factor that it is the pressure, the temperature, light, humidity, etc. They can return to their original state when this factor is removed. Commercial photochromic and thermochromic colorants that change rapidly and reversibly from colorless to colored state when activated by stimuli like ultraviolet irradiation, temperature or pH are well established class of colorants for manufacturing of niche products. We can use photochromic and thermochromic systems in applications like medical thermography, plastic strip thermometers, photochromic lenses, etc.[40] On of the example is for the use of x-chromic textile is a smart dressing, which changes color to detect injuries of handisports. This textile was developed by British researchers,[41] who found this fall intensity detector.

The purpose of this product is to detect, to inform the patient or the entourage of the handisports of (foot-chair, rugby-chair, ski sitting, etc.) in case of fall with a change of color. The same important injury as a fracture can go unnoticed if the athlete has a reduced sensitivity and this can expose him to risks.

In addition, the garment is composed of several pockets with tulle inserts stitched opposite major areas (femur, tibia, fibula, abdomen, etc.), which are put at the risk of injury. In these pockets, it is slipped a recyclable material sensitive to pressure. In the event of a fall, the fabric changes color by displaying its color in red, the intensity of which varies according to the level of pressure undergone. Thereafter, at the end of training or competition, the color of the product becomes blue. The red colors immediately inform which areas have been mistreated. This allows both to intervene faster if the risk of injury is great or not and avoid unnecessary radios if the shock is minimal.

Another example is a smart dressing for the detection of wound infections which changes color when it detects an infection. British researchers at the University of Bath in the United Kingdom have developed this product, particularly for the follow-up of burn injuries and which alerts the patient when he detects the formation of a bacterial biofilm.[42] This fabric changes color when it detects the beginning of a wound infection. Also, it shortens the detection times and helps to avoid the use of preventive medications for burn victims. Inside the dressing, it is a small capsule, impregnated with gel and releases a nontoxic dye. When he detects an increase in bacteria, it is lipid vesicles containing a fluorescent green dye. Beyond a certain threshold, the dye is released, which gives the dressing this fluorescent color. In an early stage, this functional product is a way to prevent, alert patients and medical executives in a timely manner, when lesions begin to infect bacteria. Most of the reports on smart textile for sensing without electronics are based in the doping of textile with colorimetric indicators, that change of color in response to a chemical substance. The most studied are based in the response to acids or bases. As an example, Geltmeyer et al.[43] reports a textile able to respond to strong acids vapors or solution. It is based in a UVM-7 mesoporous material containing a colorless pentamethoxy triphenyl methanol dye that become intense purple in acid media.

The mesoporous dye was loaded in a nitro resin and coated on a cotton textile maintaining its flexibility. The high intensity of the color change allows a naked eye detection, but also it can be monitorized with a colorimeter. The system revealed reversibility and resistance to washing cycles. Promphet et al.[44] developed a smart textile for the chromogenic detection of pH and lactate in sweat. The systems, deposited on cotton, in based in a composite chitosan, carboxymethyl cellulose and methyl orange and bromocresol green for pH or a lactate enzymatic assay for lactate. The pH indicator shifts from red to blue as the pH increases and a purple color appears due to lactate. The system was successfully applied to human volunteers after jogging exercise.

The systems, deposited on cotton, in based in a composite chitosan, carboxymethyl cellulose and methyl orange and bromocresol green for pH or a lactate enzymatic assay for lactate. The pH indicator shifts from red to blue as the pH increases and a purple color appears due to lactate. The system was successfully applied to human volunteers after jogging exercise. Chronic wounds are a painful problem for the elderly and diabetics.

Recent research has shown that the pH of the fluid in wounds correlates with the healing process. A pH above 8 indicates that medication is necessary, since for efficient healing, the pH should be in the range of 5 to 7. pH-sensitive indicator cotton swabs have been developed in order to obtain fast and simple information on the wound status. The swabs simultaneously enable wound cleaning and pH measurement. The indicator dye is covalently immobilized on the swabs and shows a clearly visible color change from green (ideal pH) to red (treatment necessary). This color change can be interpreted by the naked eye as well as by an optical measurement device. The pH sensitive sensor swabs are suitable for gamma-sterilisation and have already passed cytotoxicity testing as well as tests for endotoxin levels. The pH indicator cotton swabs may provide a new method to analyse the wound status and facilitate appropriate medication.[45] The sensing capabilities can be combined with other functionalities as antibacterial properties offering a bifunctional smart textile.[46] Several studies have integrated this easy transduction mechanism within textiles to endow them with added monitoring and sensing functionalities. In this respect, the FlusiTex project[47] aimed at obtaining a multi-functional wound dressing encapsulating sensing unit to monitor and closely follow with an easy readout (e.g. either colorimetric or fluorescent) different bio-markers indicative of the wound status.

A functional ink based on a dye/antibacterial ion complex deposited on a commercial membrane enables both fluorescent and colorimetric visualization of wound exudate pH values.[48, 49]

This is particularly important since several studies have pointed out the correlation of wound pH with regard to its healing/chronic status. Similar to pH values, also the glucose concentration is indicative of the wound healing stage. Dual pH/glucose sensor embedded within a functional hydrogel wound dressing is prepared by immobilizing a fluorescent pH indicator dye and an enzymatic glucose readout system on a polysaccharide matrix[50].

A fluorescent hydrogel-textile composite material has been synthesized by surface initiated photopolymerization. An indicator dye labelled hydrogel, containing drug can undergo a swelling upon changes of pH and deliver the drug or the other biological active compound to wounds or transdermal, which is followed by change in color or fluorescence. One of the monomers in the hydrogel is fluorescence 1,8-naphthalimide, which has yellow color and emits yellow-green fluorescence. When the hydrogel responses with swelling/deswelling to environmental stimuli as pH variation, this 1,8-naphthalimide as a fluorescence sensor transducer reacts with changes in the optical properties of the hydrogel. The swelling of the hydrogel in acidic pH decreases the fluorescent intensity but increases the color intensity of the material. In alkaline pH the hydrogel reversibly shrinks what leads to changes in its fluorescent and color characteristics[51].

Colorimetric textile sensors can also be utilized as gas sensors to detect concentration of harmful chemicals and in breath analysis. Paradigmatic is the detection of ammonia, where its continuous monitoring is required to assess the occupational chronic and acute exposure to this chemical. In addition, its presence in the breath is indicative of chronic kidney disease (e.g. uremic breath). Colorimetric detection of ammonia has been recently developed by embedding a Förster resonance energy transfer donor-acceptor pair based on fluorescein and carbonaceous fluorescent nanoparticles.

Interestingly, once this pair is embedded within a silicon coating and deposited on a superhydrophobic electrospun membrane, detection of ammonia up to the low ppb level can be attained.[52]

3. SMART TEXTILES FOR MEDICAL TREATMENT

Smart textiles for therapeutic purposes are the most specialized systems for medical applications. The goal is to achieve healing. Patients can receive more consistent treatment dosages than with standard mechanisms by wearing these devices, which could be useful in applications such as drug delivery, pain management, asthma management, and insulin delivery for various chronic disorders (e.g. chronic pain, bedsores and ulcers, asthma, COPD, diabetes, etc.).

3.1 Smart textiles for medical treatment obtained by integrating electronics

In this part, some examples on the smart electronic textiles used for medical treatment are pointed out. The PHOS-ISTOS[53] project has been funded by Europe in the 7th Framework Program in 2013. The aim of the project to develop an alternative method to photodynamic therapy for the treatment of pre-cancerous skin condition Actinic Keratosis. The collaboration between INSERM, MDB Texinov and ENSAIT resulted in development of a light emitting textile which can is developed to replace the rigid LED panels.[54] Plastic optical fibers are woven or knitted to create a flexible, homogenous light emitting fabric and connected to a specific light source. The novel device "Fluxmedicare" is flexible and ambulatory.

The flexibility of the device gives the possibility to adapt patient morphology which makes the light emission more homogeneous, where the light emission power was less necessary so the pain of the treatment.[55] The portability of the device gives the possibility to decrease the costs of the treatment and treat more patients in the same time. Furthermore, this development is applicable in many different treatments like for jaundice of new born, fluorescence diagnosis etc.

Figure 7 - NeoMedLight - medical devices for phototherapy for treating neonatal jaundice

Another example is from NeoMedLight, which is a company that develops medical devices for phototherapy. They have developed "Bilicocoon" to treat neonatal jaundice in collaboration with Brochier Technologies.[56] The device has 2 parts: light emitting textile woven with optical fibers and a light source. Furthermore, this device may be used in mucositis, dermatitis, wound healing/tissue regeneration and pain management issues.

One of the benefits of this technology is that it permits the newborn to be kept next to the mother in the first hours while the mother can continue to holding the baby or breastfeeding.A similar approach has been developed at Empa using melt-spun POFs.[57] In this concept, however, no treatment of the fiber was required, as light-outcoupling was obtained by optimizing the weaving patterns of the POFs. The project resulted in a proof-of-concept prototype.[58] Engineers at the Wyss Institute for Biologically Inspired Engineering at Harvard University have developed smart textile-based soft robotic exosuits that can be worn by soldiers, rescue workers and fire fighters, and also help elderlies and people suffering from neurodegenerative disorders to enhance their mobility.[59]

3. 2 Smart textiles for medical treatment without electronics Smart wound-care materials

3. 2. 1 Smart wound-care materials

Wound healing is a multi-phases and multi-factorial physiological process. To achieve an ideal wound care product, which may be classified as 'smart', it is necessary to understand the processes that occur on the injured surface like inflammation, epidermal regeneration etc. The following characteristics are required for the ideal modern and smart wound-care material: bio adhesiveness to the wound surface, ease of applications, easily sterilized, inhibition of microbial invasion, ease of wound exudate removal, biodegradability, biocompatibility, oxygen permeability, non-toxicity, low cost etc.

Biomarkers and smart wound dressing

Biological factors and microenvironment play a crucial role in wound healing process, understanding of wound biomarkers can help to accelerate this process. Textile materials modified with bioresponsive hydrogel have many advantages as wound dressing for chronic wounds. Upon swelling hydrogel can absorb excess of exudate, keeping the wound environment moist and at the same time absorb proteases, sequestration of cofactors and can also release inhibitory components capable of reducing enzyme activity depending on wound requirements.

Recently, an optical biosensor based on porous silicon resonant microcavity structure modified with fluorogenic peptide substrate was used as a potential point-of-care diagnostic tool for biomarkers of bacterial wound infection.[60]

A new perspective in the field of wound dressing is embedding the nanoparticles into a hydrogel. A new composite materials cotton fabric-hydrogel-nanoparticles (Silver, Zinc oxide or Barium hexaferrite) have been obtained via surface initiated photopolymerization to control the spread of infections.

Biomarkers and smart wound dressing

Nowadays, dressings may contain different types of sensors that besides being mechanically flexible, breathable, easy to apply, also should be capable of reporting quantitative information about the wound status in real time to guide treatment decisions. Very recently, Pal et al. (2018) proposed to incorporate the low-cost electrochemical and impedance sensors, fabricated using omniphobic paper, into commercially available bandages to monitor the status of open chronic wounds and pressure ulcers.

Temperature-sensitive wound dressings

It is known that temperature may have a beneficial influence on wound healing. All cellular functions, especially enzymatic and biochemical reactions, are optimized at normal body temperature. In recent studies poly-N-isopropylacrylamide, a polymer which is able to assimilate water under strictly defined conditions, was used for a fabrication of temperature-sensitive wound dressings. Its lower critical solution temperature is set at 32-33°C, below this point it absorbs water and extends its chain conformation, above 32°C, in an aqueous solution, it is extensively dehydrated and compact. The wound dressing transferred the fibroblast cell sheet to skin surface of the wound and also encouraged temperature-based wound healing.[61] Thermo-responsive hydrogels based non-adherent wound dressings were prepared with poly(N-isopropylacrylamide) and reinforced with cellulose nanocrystals via free-radical polymerisation reaction.[62] Very recently, a multifunctional hybrid hydrogel-based wound dressing was prepared with anti-protein adsorption and antibacterial properties. The methacrylate arginine and N-isopropylacrylamide were polymerised by free-radical reaction and crosslinked to produce the hydrogel.[63]

Bioactive dressings

These dressings are known for their biocompatibility, biodegradability and non-toxic nature and are derived generally from human, animal or plant sources such as collagen, hyaluronic acid, chitosan, alginate and elastin etc. Polymers of these materials are used alone or in combination depending on the nature and type of wound. Biological dressings are sometimes incorporated with growth factors and antimicrobials to enhance wound healing process.[64]

Tissue-engineered 'skin equivalents'

One of the advanced treatments for improving the healing of chronic or non-healing ulcer is the usage of tissue-engineered skin equivalents, e.g., Dermagraft[65] (Advanced Biohealing Inc, Lojalla, CA, USA) and Apligraft[66] (Organogenesis, Canton, MA, USA). These dressings are polylactin and collagen-based scaffolds seeded with keratinocytes and/or fibroblasts.

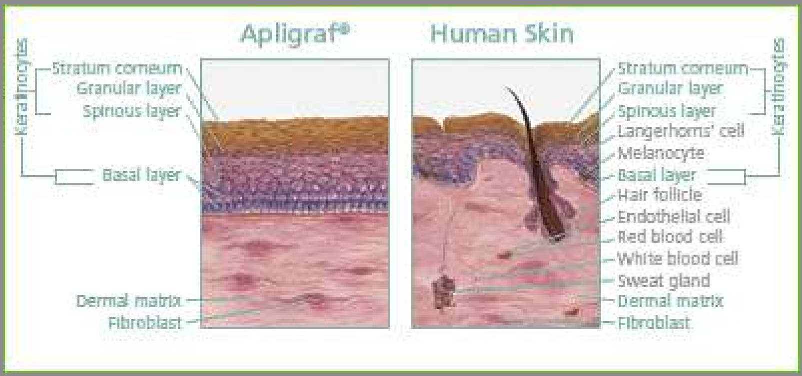

Figure 8 Apligraf - living, bi-layered cell based product to heal both Diabetic Foot Ulcers and Venous Leg Ulcers

The reconstruction of skin in tissue engineering has been mainly focused on the development of stratified constructs mimicking the bilayered structure of the epidermis and dermis.

Conventional fabrication techniques such as manual dispensing, molding, freeze drying, and porogen leaching have been used extensively in skin tissue engineering for the fabrication of cellular scaffolds.[67, 68] Novel approaches have used free-form deposition[69] to miniaturize in vitro models. Although easy to implement, they lack the engineering control required to fabricate architecturally complex tissues.[70] Bioprinting which refers to the 3D printing of biological materials and cells for the generation of living tissue enables precise layer-by-layer deposition and fabrication of complex designs. Owing to the highly stratified and complex structure of the skin, bioprinting offers unique advantages for developing clinically relevant skin constructs that capture native heterogeneity and architecture.

Medical treatments that deal with healing processes are of great importance for dental interventions. The one of the most important procedures in periodontology is the preservation of the supporting apparatus of the tooth. Aggressive forms of periodontal disease are reflected in the great loss of bone tissue so that one of the main methods of treatment is the so-called guided bone regeneration and involves the use of bio membranes that can be made from smart textile. The desirable characteristics of the membrane utilized for guided bone regeneration (GBR) therapy include biocompatibility, cell-occlusion[71] properties, integration by the host tissues, clinical manageability, space-making ability, and adequate mechanical and physical properties.

With the aim to develop a novel membrane with an appropriate mechanical property and degradation rate for guided bone tissue regeneration, lyophilized and densified silk fibroin membrane was fabricated and its mechanical behavior as well as biodegradation property were investigated.[72]

3. 2. 2 Textile-based drug release systems

Textile-based drug-release systems can overcome many of the shortcomings associated with the traditional drug administrations like ointments, injections, pills, etc. When a drug is administered orally, they undergo hepatic metabolism, as a result of which the concentration of the drug available at the site of absorption decreases. When the dose is administered trans dermally the amount of drug that is administered is reduced. Also, this route of administration is useful when the patient is unconscious, finds hard to swallow, infants, etc. Drug-releasing textiles can be divided into three main categories: woven fabrics, non-woven fabrics and non-woven electrospun fabrics.

→ Woven fabrics

In general, woven fabrics will have drugs that are physically absorbed or adsorbed, coated, encapsulated, or covalently bound to the fabric surface. Medicated woven fabrics offer precise geometry, pore structure, or strength that is suitable for a variety of medical applications apart from the drug-eluting properties. Drug-loaded woven fabrics are commonly used as bioactive bandages, artificial skin grafts, scaffolds for tissue repair or regeneration, aromatherapy, and many other applications.[73] Lately, much efforts have been made to develop antimicrobial wound dressings impregnated with metal nanoparticles (silver and copper-based) with controlled release and low cytotoxicity for healing of acute and chronic wounds.[74]

Non-woven fabrics

Drug-encapsulated non-woven fabrics are produced by putting small fibers together in the form of sheets or web-like structures following entangling of drug-loaded fibers or filaments mechanically, thermally, or chemically. Non-woven drug-release structures are particularly suitable for controlled and sustained release applications because of their 3D structure and the use of fibers of defined porosity and geometry.

Non-woven electrospun fabrics

Electrospun nanofiber scaffolds were very recently used for new potential treatment strategy against cancer. Kumar et al.,[75] fabricated electrospun biodegradable PLA scaffolds embed with drugs for tumor treatment without any toxic side effects. Various methodologies are employed in the immobilization of bioactive agents and drugs onto the textile surfaces: coating methods, encapsulation, bioconjugation.

Coating methods

Coating is a common approach that allows direct application of the drug onto the fabric surface either by dipping in drug solution or by coating with drug encapsulated in micro- and nanoparticles.

Encapsulation

Encapsulation of drugs and active ingredients in various textile structures can be best carried out at the fiber preparation stage. The encapsulation approach basically involves dissolution of the polymer and the active ingredient in a common solvent followed by spinning of the solution into fibers by suitable techniques. The technique makes it possible to load the fiber with the desired amount of active agent with uniform distribution throughout the textile structure.
Electrospun fibers of polyurethane (PU) and (PU/HPC) with or without drug loaded were successfully fabricated by electrospinning technique. The structures of the PU/hydroxypropyl cellulose (HPC) electrospun fiber loaded with Donepezil (DP) which is used for the Alzheimer Disease, were characterized using Fourier Transform Infrared Spectroscopy (FTIR). UV-Visible spectrophotometer and Electrochemical Impedance Spectroscopy (EIS) are used to determine drug release from the electrospun fiber in buffer solution.[76]

Bioconjugation

In addition to encapsulation, the bioconjugation process can be used to couple the bioactive agents to the textile surface via chemical or physical methods to prepare drug-releasing textiles. To achieve conjugation the textile must be made amenable to the bioactive agent/drug by functionalization of its surface. Many suitable techniques are available, which include plasma treatment, chemical activation, and grafting.

3. 2. 3 Textile-based drug release systems

Fibrous scaffolds have been extensively used in regenerative medicine applications. Specifically, biomedical textiles with fibrous structure have a long history in treatment, repair, and replacement of tissues. Due to the similarity of the medical textiles based fibrous scaffolds to the extracellular matrix (ECM) structure, these constructs are attracting noticeable attention for the tissue engineering (TE) applications. Researchers in the field of polymer science, textile, and fiber technologies have attempted to develop different fabrication methods and to synthetize materials for soft tissues TE.

Currently some of the commercial biomedical textile products, available in the market, are TIGR Matrix[77] (to reconstruct the breast tissue after cancer or as an abdominal wall closure) developed by Novus Scientific, Uppsala, Sweden; ULTRAPRO ADVANCED[78] (inguinal and ventral hernia repair), produced by Ethicon US, LLC, USA; and INTERGARD SILVER[79] (as woven/knitted vascular grafts) created by Maquet GETINGE Group in Rastatt, Germany.

Different designs (e.g., woven, knitted, and bioprinted) provide specific structural and mechanical properties for the scaffolds, which are appropriate for tissue regeneration or replacement.

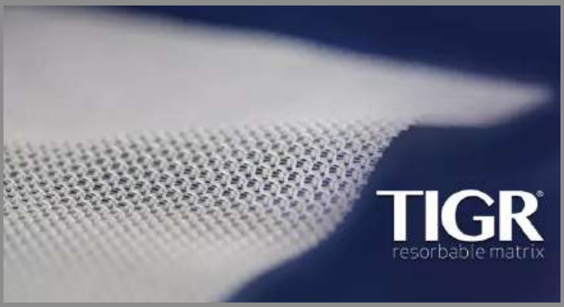

Figure 9 – TIGR Matrix- resorbable matrix which reconstruct the breast tissue after cancer

Woven Fabrics

Woven fabrics are widely used in TE as scaffolds or as reinforcement mats in hydrogels to improve the mechanical properties of the structure. In a pioneering study, Moutos et al.[80] used a 3D weaving approach to create poly (glycolic acid) (PGA) yarns into fabrics in which various layers of the fabric were interlocked to enhance the through-plane load-bearing properties. In this study, chondrocyte-laden agarose gel was reinforced with woven fabric of PGA for cartilage TE. Other groups have also fabricated reinforcing structures from different materials such as silk, polycaprolactone (PCL), and polypropylene using similar approaches.[81, 82] Recently, few efforts have been made to assemble cell-laden fibers to create woven fabrics with tunable mechanical properties and to control the cellular distribution. In this case, hydrogel fibers were used as cell carriers and then assembled as part of the fabrics.[83] To overcome the challenge of low mechanical properties of the hydrogel fibers and to facilitate the assembly process, composite fibers with a load-bearing core polymer and cell-laden hydrogel in shell have been fabricated.[84]

Knitted Fabrics

The fabrication process is very attractive for use as TE scaffolds due to the variability of the fabric and robustness of the knitted scaffolds fabrication process. Due to excessive mechanical stresses that fibers experience during the assembly process, knitting of cell-laden hydrogel fibers has been a major challenge. However, recently, the development of cell-laden composite fibers has enabled their assembly into 3D knitted fabrics by developing new knitting machines equipped with computer aided design (CAD) systems which have resulted in 3D constructs with defined microstructure.[85] However, fabrication of multicellular patterns with tunable property in different directions has still remained a challenge.

Braided Fabrics

Braiding is a textile process consisting of more than three fibers or threads intertwined. Braided constructs offer high axial and radial load-bearing properties in comparison to the other textile constructs.[86, 87]

Braided constructs are usually fabricated in circular or tubular shapes with dense walls; thus, these scaffolds have been used as sutures, stents, nerve regeneration conduits, and for other TE applications in the past. The type of material and size of the fibers control the structural and mechanical[88] characteristics of braided constructs. However, high density of the fibers and small pores of the constructs are the challenges to overcome for efficient cell penetration through the braided fabrics. To address these issues and eliminate the need for cell infiltration, cell-laden fibers have been braided into scaffolds during the process resulting in 3D constructs integrated with living cells. Owing to their architecture, flexibility and dimensional stability, braided conduits have also been used as nerve conduits.[89]

Non-woven fabrics

To mimic the functions of ECM, electrospun nanofibers have been extensively explored as a class of scaffolding materials, owing to their unique ability to recapitulate the composition, length scale, and architecture typically of native ECM. By combining structural guidance with cellular components and/or bioactive molecules, electrospun nanofibers can improve the repair or regeneration of various types of tissues, including the repair of nerve injury, healing of wound, patching of myocardium defect, bridging of vascular rupture, remodeling of musculoskeletal tissue, and construction of interfaces between different tissues, etc.

Electrospun nanofibers with uniaxial alignment have been extensively explored for neural tissue engineering.[90] In particular, uniaxially aligned nanofibers can provide ECM like microenvironment to direct cell alignment and neurite extension.[91] The nanofibers can be further modified with pores, grooves, or other secondary structures as additional topographic cues to promote neurite extension and/ or Schwann cell growth.[92] Scaffolds made of electrospun nanofibers have been actively explored for myocardial tissue regeneration.[93] 3D cardiac scaffolds are developed to replicate the specific 3D architecture of the myocardium.

Electrospinning has been used to fabricate cardiac scaffolds from completely decellularized porcine cardiac ECM.[94] The as-obtained scaffold was able to preserve the ECM composition, self-assemble into the same microstructure of native cardiac ECM and retain key mechanical properties.

In contrast to the case of large-diameter arteries, where there are already practical non-tissue engineered grafts, there is an urgent need to develop biomimetic scaffolds for clinically regenerating blood vessels of small sizes[95] (typically, <6 mm). Researchers have investigated the in vitro and in vivo performance of bilayer scaffolds, with one layer featuring low porosity and another layer exhibiting high porosity either on the luminal or adventitial side.[96]

Compared with the vascular scaffolds made of a single layer of nanofibers with high porosity, the bilayer scaffolds significantly reduced blood leakage, indicating that a low porosity layer is needed when constructing a multilayered vascular scaffold to achieve both good cell infiltration and low blood leakage. Within the Zurich Heart Project,[97] novel approaches are developed for enhanced pulsatile ventricular assist devices (VAD's), where the risk of thromboembolic events on the artificial surfaces in contact with blood remains a major challenge. In particular, these events limit the usage of VAD's to be applied in patients during short or mid-term therapy.[98] As found in nature, an intact autologous layer of endothelial cells possesses the best-known anticoagulant properties, and therefore mimetic materials are developed for stable and confluent attachment of functional endothelial cells, mainly based on tailored morphology, surface topography and chemistry.[99, 100]

3. 2. 4 Antibacterial smart textiles

It is well-known that 2 million people are dying annually out of bacterial infections in the Hospital. A major part by which these bacteria are transferred is by the textiles. It is therefore believed that making the textiles antibacterial will considerably reduce the infection. It I also clear that the smart antibacterial textile should sustain it properties in the same processes that the regular textile undergo in the Hospital, namely, many washings at temperatures such as 75 and 92°C.

During the Projects Lidwine[101] (FP6) and Sono (FP7)[102] a new coating technique was developed that coated various textiles with nanparticles of metal oxides such as ZnO, and CuO. The coating technique uses ultrasonic waves. The coated fabric withstood 65 washing cycles at 75°C and small losses of the coated materials were measured. The killing of S. Aureus was almost log 5.[103]

A successful experiment was carried out in a hospital where bed sheets, pillow covers, pajamas, and bed covers were all knitted from cotton coated with nanoparticles of ZnO, and 21 patients were dressed and slept on these fabrics. The control was composed of 16 patients that dressed and slept on regular cotton fabrics. A distinct difference in bacterial contamination was detected in the comparison between the two populations.[104]

4. OPPORTUNITIES AND TRENDS

This paper gave an overview of the potential of smart textiles for healthcare & medicine. The global market for smart textile is projected to show a strong growth in the next 5 years, fueled by technological, demographic, economic, and business trends indicating that these growth rates may continue or even accelerate in the years beyond.

For example, according to Allied Market Research,[105] the global smart textile market size is expected to reach $5.4B by 2022 from $943 million in 2015 at a CAGR of 28.4% from 2016 to 2022, while IDTEchEx expects a lower $2B by 2029.[106] More in details, Market Research Future (MRFR), set a CAGR of 9.5% over the 2018-2027 period for the global medical smart textile market.[107]

Continuous heart rate monitoring is a growing area in healthcare, as well as systems for diabetic patients, such as glucose-sensing devices and insulin-delivery carriers for optimized dosage of insulin according to detected glycemic levels, which are anticipated to dramatically change diabetes management and patient monitoring. Most of the applications can thus be found in hygiene, surgery, therapy, drug-release systems, wellness, and biomonitoring.

In the future, the release of different drugs could be controlled in response to signals collected by biosensors based on different reactions by the human body. Certain technical challenges still need to be tackled for smart textile to be adopted and deployed widely in the future.[108]

For example, systems should be capable of operating under different conditions, such as in humid or wet environments and in warm temperatures, without losing performance during activities like swimming, showering or sunbathing. Smart textiles and stretchable electronics demand washability and dryability and the electrodes must not break when the device is folded or bent. Moreover, the need to meet the strict regulations for medical devices, which are heavily regulated due to their safety implications and functional requirements, is something that should be taken into account in the future when bringing the smart textile systems from laboratory testing environments to the market.

5. CONCLUSIONS

Smart textiles find variety of applications in healthcare and medicine from sensors and actuators through wound-care materials, drug-release systems to tissue engineering scaffolds. By using smart textiles, advanced solutions for sensing, monitoring and actuating are made available. Sensors can be placed throughout the fabric of the clothing in order to get a detailed report of the status of the individual including heart rate, breathing rate, sweat rate, posture, and movement related information. They support the healing processes, improving safety and comfort of living of the patients ensuring their mobility in a friendly way while collecting the data. At present from the whole variety of textile sensors and actuators for healthcare, textile electrodes are those that are mostly commercially introduced due to the availability of the materials and well-developed technological approach. But also, there are a great number of offered solutions and scenarios for manufacturing textile biosensors that are still at the prototyping stage. Some products are already accepted by the industry and introduced to the market, but the process of development technology transfer to manufacturing is burden due to the high costs of fabrication, and commercial introduction and use.

Wound care materials have a very fast rate of development. In the past, people mostly considered the protective function of dressings, but today, they are loaded with drugs, different sensors and devices. On the basis of the achievements of current techniques and science, we can imagine that in the future, structures and applications of wound-care products will become more and more sophisticated, and patients' recovery to health will be faster, painless and continually monitored. Smart textiles hold a great promise for applications in tissue engineering and regenerative medicine. The versatility of textile techniques provides exciting opportunities in engineering scaffolds and tissue-like structures with controlled microarchitecture and cellular distribution. Textiles are highly porous and permeable to nutrients, oxygen, and growth factors. Textile tissue engineering allows simultaneous control of mechanical properties and cell distribution within a construct.

But before smart textiles for tissue engineering can be used in the clinical setting there are a number of significant challenges that must be overcome and it may take many years, in some cases, before these technological breakthroughs are available commercially, since the process for FDA approval is arduous and expensive. In spite of significant amount and qualitative and quantitative innovation in medical textiles, this sector is still at a nascent stage. The medical textile market will develop, in the terms of commercialization, in the years to come because it has a huge untapped potential yet to be discovered and explored.

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