International Journal of Engineering and Technical Research (IJETR)
ISSN: 2321-0869, Volume-2, Issue-2, April 2015

Medical applications of biomimetic materials as a synthetic nerve guide implants and optical fiber as sensor systems.

Salikhova M.A, Morozov O.G.

***Abstract*—Extensive damage of the nervous system usually leads to the loss of sensory and motor functions. It can be permanent or temporary, depends on damage level. In that case, such thing as nerve guide implants can be found useful.**

Depending on of the damaged site, various donor nerves may be used for grafting sacrificing native functions in their target areas. Recently, several synthetic nerve guide implants have been introduced and approved for clinical test use as mean to replace autologous transplants. This alternative therapy based on pioneering studies with experimental nerve guides such as biomimetic materials. But not only biomimetic materials can be used as a nerve guide. The intrinsic physical characteristics of optical fiber combined with its versatility in remote sensing make it an attractive technology for biomedical applications as well. Point is – that combine use of both biomimetic materials and optical fiber if possible to achieve can prove itself as even more advanced and evolve nerve guide implants.

***Index Terms*—biomimetic, optical fiber, implants, regeneration, medicine.**

I. INTRODUCTION

The highly debilitating nature of spinal cord injuries has provided much inspiration for design of biomaterials that can be used to stimulate cellular regeneration and its functional recovery. Injuries to the spinal cord pose a significant healthcare problem. Symptoms of spinal cord injury can vary in severity and often become highly debilitating. Early beliefs led to conclusion that damaged nerves in the central nervous system (CNS) lacked the intrinsic ability to regenerate. But still, research showed that spinal cord nerves can partially regrow into peripheral nerve grafts (Richardson et al., 1980).

Therefore current clinical treatments are generally limited to reduction of pain and swelling and the prevention of secondary injuries through the administration of anti-inflammatory drugs such as methylprednisolone (Bracken et al., 1990) [1]. However use of fiber optic sensors (FOSs) with a particular reference to biomedical applications is also developed in quite a technique. Fiber optic technology is opening exciting new fields of application in the medical industry. Miniaturization and the availability of plug and play and easy-to-use devices are the main reasons of the growth that is taking place in the use of FOSs.

Many experts [1] agree that the greatest hope for treatment of nerve injuries will involve a combinatorial approach that integrates biomaterial (scaffolds), cell transplantation, molecule delivery and bio-nano technical means. This article is review of already existing methods and means of treatment.

II. TISSUE ENGINEERING

Tissue Engineering is a rapidly evolving field in terms of cell source and scaffold fabrication. As the template for three dimensional tissue growths, the scaffold supposed to emulate the native extracellular matrix, which is nano-fibrous [3].

Here are three basic techniques capable of generating nano-fibrous scaffolding. First - electrospinning, second - molecular self-assembly, and third - thermally induced phase separation [2]. Scaffolds can be further modified by various three dimensional surface modification techniques and, if necessary, to more precisely emulate the native extracellular matrix. There are three basic approaches to tissue engineering [2]:

- Use of isolated cells or cell substitutes to replace the cells that supply a needed function;
- Delivery of tissue-inducing substances such as growth factors to a targeted location;
- Growing cells in a three-dimensional scaffold.

For small, well-contained defects the first two approaches may be suitable. However, to produce a larger blocks of tissue with predesigned shapes only the third approach, (using a scaffold to direct cell growth) can be sufficient. It’s lead to the conclusion, that both cells and materials play an important role in de novo tissue development.

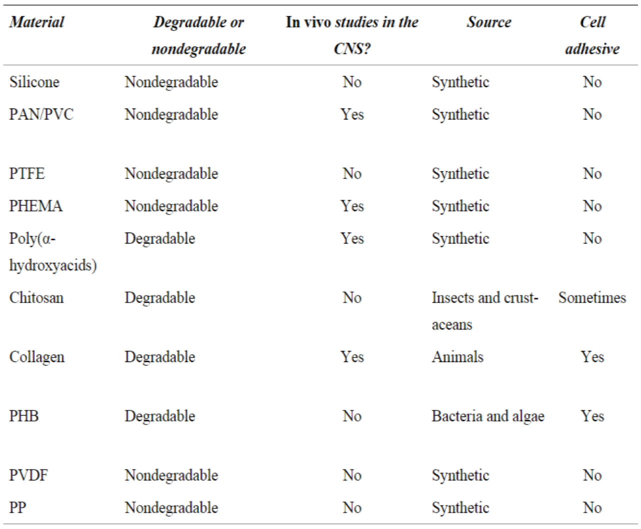
Still, even without further modification, nano-fibrous scaffolds have been shown to have advantageous effects on cellular behavior and tissue formation when compared to more traditional types of scaffolding.

III. NERVE GUIDANCE CHANNELS

Nerve guidance channels can be synthesized from a wide assortment of natural (degradable) and synthetic (nondegradable/degradable) polymers for CNS (central nerve system) treatment (Figure 1).

Manuscript received April 21, 2015.

Salikhova M.A, Salikhova Marina. Kazan National Research Technical University named after A.N.Tupolev (KNRTU-KAI), Russia, Kazan
Morozov O.G., Morozov Oleg Kazan National Research Technical University named after A.N.Tupolev (KNRTU-KAI), Russia, Kazan



Material	*Degradable or nondegradable*	In *vivo studies in the CNS?*	*Source*	*Cell adhesive*
Silicone	Nondegradable	No	Synthetic	No
PAN/PVC	Nondegradable	Yes	Synthetic	No
PTFE	Nondegradable	No	Synthetic	No
PHEMA	Nondegradable	Yes	Synthetic	No
Poly(α-hydroxyacids)	Degradable	Yes	Synthetic	No
Chitosan	Degradable	No	Insects and crustaceans	Sometimes
Collagen	Degradable	Yes	Animals	Yes
PHB	Degradable	No	Bacteria and algae	Yes
PVDF	Nondegradable	No	Synthetic	No
PP	Nondegradable	No	Synthetic	No

Fig. 1 Common Materials Used to Construct Nerve Guidance Channels [4]

The nerve guidance channel serves to prevent the ingrowth of fibrous scar tissue. To concentrate neurotrophic molecules released from the injured nerve stumps, and to direct growth from the proximal to the distal nerve stump (Danielsen et al., 1993; Longo et al., 1983; Lundborg et al., 1982; Williams et al., 1983).

The dimensions, material of construction, and luminal components all affect the regenerative capacity of a given nerve guidance channel design. Several materials have already been approved by the FDA for use in the repair of short gaps in human peripheral nerves (Schlosshauer et al., 2006) [4 Table 2]. In 2010, most research involving nerve guidance channels has already involved PNS applications. However, encouraging results demonstrating partial CNS nerve regeneration in PNS guidance channels have led to increased interest in their use for spinal cord repair [2].

Since no material has currently established itself as a clear or dominant choice for either PNS or CNS repair, there is still a large demand for new materials. The choice of material for use in nerve guidance channels has largely been influenced by the underlying regeneration strategy [4]. Central to the choice of regeneration strategy is the distinction between using nondegradable (and generally "bioinert") grafts versus biodegradable (and generally "biointeractive") grafts [3].

Nondegradable channels are made of synthetic materials that offer uniform and controlled synthesis techniques. Though they require a less complex design due to the lack of issues such as degradation rate control and toxicity of degradation products but the permanent implantation of a nondegradable channel creates a higher risk of inflammation and may result in nerve compression over time, which often necessitates a second surgery to remove the material (Belkas et al., 2005; Mackinnon et al., 1984; Merle et al., 1989) [4].

Nondegradable materials are almost always inherently non-cell adhesive which is limiting their application in more advanced channel designs involving cell transplantation. Despite these inherent limitations, the simplified design and construction of nondegradable channels have made them particularly useful in preliminary studies of CNS nerve repair and have sped up experimental progress through their use both in vitro and in vivo [4].

Degradable channels circumvent the need to either permanently implant a nondegradable material or remove a nondegradable material with a second surgery. They also present a smaller risk of nerve compression, since they degrade as the nerve regenerates [4].

Degradable channels can be composed of either natural or synthetic materials, but the majority of degradable channels come from natural sources. Materials harvested from natural sources can present problems in uniformity and controlled fabrication of nerve guides due to batch-to-batch variability. Furthermore, many naturally harvested materials are difficult to purify, and incomplete purification can result in immune-system activation by the implant.

Degradable channels also require more complex designs that nondegradable, Reasons are - degradation products must be nontoxic and their degradation rates must be tuned to match the regeneration rate. Natural materials are often more inherently adhesive to neurons and glial cells, making them candidates for more "biointeractive" designs [1]. Some common degradable materials that have been studied for use in nerve guidance channels include the polymer family of poly(α-hydroxyacids), collagen, chitosan, and poly(β-hydroxybutyrate) (PHB) [5].

IV. FIBER OPTICS IN MEDICINE

Fiber optic sensors have numerous applications in diverse branches of science and engineering, as is evident from a vast range of properties which has been sensed optically, ranging from light intensity, vibration, temperature, pressure, calibration of accelerometers, strain, liquid level, pH, chemical analysis, concentration, density, refractive index of liquids etc[7]. Refractometer are frequently used for the study of molecular structure and identification of organic compounds [7, 8].

The most significant and prevalent applications of fiber optics in medicine are in the imaging and illumination components of endoscopes. Flexible and rigid multi fibers composed of step-index fibers and graded-index imaging rods are extensively used for visualization of internal organs and tissue which are accessible through natural openings or transcutaneously [6].

The fabrication techniques of optical fibers for imaging and illumination are considered in juxtaposition to their current applications in communications with emphasis on the different technologies involved. [7].

For example, low-loss optical fibers are employed to transmit laser energy for surgery and photocoagulation. Multicolor laser light is transmitted through a single thin optical fiber to provide adequate illumination for viewing and color photography. Past attempts to develop plastic imaging multi fibers and their future potential viewing and color photography. Other uses of fiber optics in medicine include remote spectrophotometry, pressure and position sensing, or scintillation counting.

Two types of fibers are offered for a given incident wavelength namely, mono mode and multimode. Mono mode fibers have a narrow glass core of uniform refractive index profile and transmit only a single mode for light of a specific wavelength range and linearly polarized state. Mono mode fibers produce a Gaussian spatial intensity distribution at their distal end, whereas multimode fibers have a greater core diameter and can transmit many a hundreds of light modes having either a uniform or parabolically profiled cross sectional refractive index [6].

It is much easier to commence high intensities into multimodal fibers because of their larger core size and higher numerical aperture, than their mono modal equivalents or counterparts. However they have major disadvantages such as a related to modal noise. Any thermal or mechanical annoyance to the fiber affects each transmitted mode in a diverse way. As a result, although the total light intensity at the fiber exit remains constant, the far field radiation pattern formed by intervention of these modes changes with time [7].

V. HELPFUL HINTS

Biomedical sensors present unique design challenges and particular problems related to their interface with a biological organism. Sensors must not only be safe, reliable, highly stable, biocompatible but also amenable to sterilization and autoclaving, not prone for biologic rejection, and not require calibration (or at least not miscalibration easily). The devices also must be as simple as possible.

Applications for biomedical sensors can be classified as in vivo or in vitro. From the perspective of how sensors are applied to a patient or biological system, they can be classified as noninvasive, contacting (skin surface), minimally invasive (indwelling), or invasive (implantable) [11]. Biomedical sensors can be used in human’s clinics, animal’s vets, or other life science connected fields.

Depending on the intended it can be used for diagnostic, therapeutic, or intensive care uses in clinical applications; research and preclinical development; or laboratory testing. Below are listed few examples of optical fiber sensors used in medicine:

Luminescent optical fiber sensors - use of luminescent phenomena, directed chiefly on fluorescence for optical sensing, has been observed with a range of diverse fiber hosts. However, unlike the plastic host that has disadvantage of quenching laser action, there are ample varieties of other fluorescent materials which can be used for sensing purpose, where their primary focus is only on the fluorescence. A key distinction between silica and plastic fiber is the extreme elasticity of the latter, which allows it to bend to a greater extent with a smaller radius than silica fiber [6].

Evanescent wave fluorescent sensor - negative or non-guiding fiber is a permeable fiber in which the power loss depends on the length of the fiber and can be optimized for fluorescence collection efficiency into the positive or guiding fiber attached to the output end of the negative fiber. As a contrast to the positive fiber for which the collection efficiency is independent of fiber length and depends only on the difference in refractive index between core and cladding material of the fiber. The sensor described is based on a fiber having two different fibers, one guiding and other non-guiding. [6].

Fluorescent plastic optical fiber sensors - this category are characteristically doped with organic dyes which are used extensively in the printing industry and for display purposes. It’s are frequently used for decorative purposes, but clad (dressed) and coated fibers with a fluorescent core are often used in sensing and measurement as a result of their ability to capture light, which excites them over their whole length. The kind of fluorescent sensors are used to measure ambient light (Grattan K, Meggitt B. 2000), monitor faults in circuits and switches (Augousti AT, Mason J, 1990), humidity measurement, environment sensing and detection of gaseous pollutants [6].

Fiber-optic biomedical sensors – such sensors comprise an optical fiber, external transducer, and photodetector. They sense by detecting the modulation of one or more of the properties of light that is guided inside the fiber—intensity, wavelength, or polarization, for instance. The modulation is produced in a direct and repeatable fashion by an external perturbation caused by the physical parameter to be measured. The measured of interest is inferred from changes detected in the light property [11].

Fiber-optic sensors can be *intrinsic or extrinsic*. In an intrinsic sensor, the light never leaves the fiber and the parameter of interest affects a property of the light propagating through the fiber by acting directly on the fiber itself. In an extrinsic sensor, the perturbation acts on a transducer and the optical fiber simply transmits light to and from the sensing location.

In terms of sensor development, the basic imaging sensors are the most developed [10]. Fiber-optic sensors for measurement of physical parameters are the next most prevalent, and the least developed area in terms of successful products is sensors for biochemical sensing, even though many FOS concepts have been demonstrated [12].

Among the latest development efforts are shape-sensing systems that use arrays of FBGs disposed along multicore, single mode fibers. The FBGs can shift peaks of wavelengths in response to the strain and curvature stress produced during bending. The fibers arrays help determine the precise position and shape of medical tools and robotic arms used during MIS.

Other applications - it is possible to construct the use of filtered fiber optic Raman probes include such things as measuring high levels of organic solvent contaminants in soils and aquifers, chemical process monitoring of petrochemicals and distillation products, monitoring polymer cure reactions in situ and many others [13-14].

In spectroscopy, in order to analyze the composition of substance that cannot be placed into the spectrometer itself can be measured by optical bundles by transmitting the light from a spectrometer to a substance. A spectrometer analyzes substances by bouncing light off of and through them. By using fibers, a spectrometer can be used to study objects that are too large to fit inside, or gases, or reactions which occur in pressure vessels [11].

VI. CONCLUSION

Biomedical/biomimetical materials application represents a advanced and growing opportunity for nerve injures treatment, particularly for combine of both nerve guide conducts and optical fiber sensors. The demand for more patient monitoring devices combines with a trend toward minimally invasive surgery, which itself requires a variety of minimally invasive medical devices as well as single-use, disposable sensors of small size that can be incorporated into catheters and endoscopes—an ideal fit for fiber-optic sensors as well as need for compatible nondegradable/degradable are also take place. There is also an unquestionable opportunity for FOS as EMI-compatible sensors to monitor vital signs during use of MRI (and related techniques), and use of silicon or ever spider silk layering for guidance constructs.

Sensor design and development is not trivial, and proper material selection, design, biocompatibility, patient safety, and other issues must be taken into account as well as naturally inhibitory environment of CNS injury sites still presents a difficult problem for the field of tissue engineering. It is believed that a highly integrated approach that attempts to mimic the permissive ECM environment seen during development may have the most potential for success.

Optimization of such a large number of design parameters and the large variety of materials currently being studied makes progress difficult. To expedite this process, recent work has involved the development of approaches to systematically compare already developed materials. Progress toward the design and optimization may potentially be hastened through more collaboration between biomimetic and optical fiber.

REFERENCES

[1] Schlosshauer B, Dreesmann L, Schaller HE, Sinis N. “Synthetic nerve guide implants in humans: a comprehensive survey”. Neurosurgery. 2006 Oct;59(4):740-7;

[2] Laura A. Smith,a Xiaohua Liu,b and Peter X. Ma “Tissue Engineering with Nano-Fibrous Scaffolds” Soft Matter. 2008 Jan 1; 4(11): 2144–2149. doi: 10.1039/b807088c

[3] Nerve guidance conduit. Available: http://en.wikipedia.org/wiki/Nerve_guidance_conduit#Biomimetic_materials

[4] Karin S. Straley, Cheryl Wong Po Foo, and Sarah C. “Biomaterial Design Strategies for the Treatment of Spinal Cord Injuries” Neurotrauma. 2010 Jan; 27(1): 1–19. PMCID: PMC2924783

[5] Gautier S.E. Oudega M. Fragoso M. Chapon P. Plant G.W. Bunge M.B. Parel J.M. Poly(α-hydroxyacids) for application in the spinal cord: Resorbability and biocompatibility with adult rat Schwann cells and spinal cord. J. Biomed. Mater. Res. 1998;42:642–654

[6] R. Y. Shah and Y. K. Agrawal “Introduction to fiber optics: Sensors for biomedical applications” Indian J Pharm Sci. 2011 Jan-Feb; 73(1): 17–22.

[7] Macfadyen AJ, Jennings BR. “Fibre optic systems for dynamic light scattering – a review.” Optics Laser Technol. 1990;22:175–87.

[8] You, F. T. S & Yin, S. (2002). Fiber Optic Sensors, Marcel Dekker, Inc., ISBN: 0-8247-0732-X, New York, NY.

[9] B. Culshaw and J. Dakin, Eds, Optical Fiber Sensors: Systems and Applications, Vol. II, Artech House (1989).

[10] F. Baldini, A. Giannetti, A.A. Mencaglia, and C. Trono, "Fiber Optic sensors for Biomedical Applications." Curr. Anal. Chem., 4, 378-390 (2008).

[11] Alexis Mendez “Medical applications of fiber-optics: Optical fiber sees growth as medical sensors” Jan 2011 Available:: http://www.laserfocusworld.com/articles/2011/01/

[12] Grattan KT, Sun T. Fiber optic sensor technology: An overview. Sens Actuators. 2008;82:40–61.

[13] Garrison AA, Moore CF, Roberts MJ, Hall PD. Distillation process control using fourier tranform raman spectroscopy. Process Control Qual. 1992;3:57–63.

[14] Mosheky Z, Melling PJ, Thomson MA. In situ real time monitoring of a fermentation reaction using a fiber optic FT-IR probe. Spectroscopy. 2001;16:15. Available: http://www.remspec.com/pdfs/SP5619.pdf