

Impacted uterine myoma in a 14 week pregnant patient

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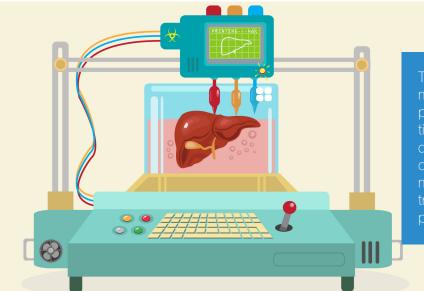
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Tissue engineering and regenerative medicine methods are extremely promising, in particular bioprinting of tissues and organs, which begun to develop at the beginning of the XXI century. Currently, medical community, have already transplanted trachea and bladder printed on a 3D printer.

Bionic Pancreas and Bionic Organs – how far we are from the success

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ABSTRACT

The progress in the treatment of chronic diseases of civilization that occurred in recent years, led to a significant prolongation of median survival time of the developed countries societies. Organ transplantation has revolutionized medicine as it became possible to replace an irreversibly diseased organ. However, at the moment we can observe a significant shortage of organs for transplantation, which forces doctors to accept those coming from more and more expanding criteria donors. No doubt, the number of donors, at best, will certainly not grow. Tissue engineering and regenerative medicine methods are extremely promising, in particular bioprinting of tissues and organs, which begun to develop at the beginning of the XXI century. Article highlights possible future direction of organ transplantation.

he progress in the treatment of chronic diseases of civilization that occurred in recent years, led to a significant prolongation of median survival time of the developed countries societies [1,2]. Paradoxically, it has raised more medical problems such as increased number of neurodegenerative, cardiovascular diseases [2,3] and increased demand for transplantation organs [4]. In Poland alone, there are more than two and a half million diabetic patients, 200,000 of which are patients with type I diabetes [5]. According to WHO's statistics, by 2030 these numbers will double [6]. Organ transplantation has revolutionized medicine as it became possible to replace an irreversibly diseased organ. However, at the moment we can observe a significant shortage of organs for transplantation, which forces doctors to accept those coming from more and more expanding criteria donors. No doubt, the number of donors, at best, will certainly not grow. Annually, there are approximately 40 pancreas transplants in Poland. Liver and kidney transplants are more numerous, with 300 and 1000, respectively, organs transplanted each year. Pancreas transplantation has been a successful treatment of patients with diabetic complications for years, limited however to relatively small number of patients not only due to organ shortage but also due to ischemic injury of retrieved organs [7]. Injury is even more pronounced in pancreatic tissue, which is subjected to digestion processes in order to isolate the islets of Langerhans, which are especially sensitive to injury. The digestion process, by stripping the islets of their vasculature and surrounding extracellular matrix in order to isolate them and put into suspension, results in their hypoxic damage. This sequence of deleterious effects is the reason that islet transplantation has not become a common clinical treatment modality [8]. More than 50% of transplanted islets are lost during the first few days post transplant. It is possible that one of the causes of this is IBMIR - instant blood-mediated inflammatory reaction [9], leading investigators search for a new recipient sites for islet transplantation [10,11,14]. Authors have invented, performed study and introduced into clinic as the first in the world, an innovative method of endoscopic gastric submucosa islets transplantation [12,13]. The damage is also caused by deprivation of the islets of their own vasculature and extracellular matrix. "Nude" islets has higher tendency for apoptosis, which further makes that simple procedure very not effective. The medical world is developing several potential paths that can solve the problem of shortage of organs for transplantation: artificial organs [15], xenotransplantation (using organs taken from animals) [16], tissue engineering and regenerative medicine [17]. There have been first visible successes in using artificial organs, such as insulin pumps [15]. But those are not able to inhibit the development of secondary complications of diabetes, which leads to nearly 5 million deaths each year worldwide [18]. Xenotransplantation, as a treatment in humans, cannot be easily brought to the clinical phase due to the still unresolved risk of transmitting particularly dangerous zoonotic viral infections together with the cells and organs taken from animals [19]. Therefore, the development of new approaches to protect newly transplanted pancreatic islets/betacells from oxidative and inflammatory stress is critical and urgently needed. Dobrzyn et al. recently showed that endocanabinoid system, stearoyl-CoA desaturase and Wnt singnaling play a critical role in keeping pancreatic beta-cell identity and islet architecture and might be used for injury treatment [20-22].

Tissue engineering and regenerative medicine methods are extremely promising, in particular bioprinting of tissues and organs, which begun to develop at the beginning of the XXI century [23]. Currently, medical community, have already transplanted trachea and bladder printed on a 3D printer [24,25]. In addition, beyond the obvious purpose of transplantation, we may use bioprinted proteins, cells, tissues, and organs in in vitro drug trials (toxicity tests), in clinical trials and in "personalized medicine", adapting the drug dosage to the biological capabilities of the potential patient's tissues. Possible rebuilding extracellular matrix, with bioprinting, for islets and creating a stable, well oxygenated scaffold might effectively improve islet transplants survival, make this treatment available for a wider population of patients and influence positively survival and quality of life of millions of diabetic patients. Building scaffolds for clinical use [32-34] in orthopaedics and oncologic surgery is also developing. Recently, there has been a significant progress in the development of scaffolds, that could constitute building blocks for organs culture with a use of stem cells [26-28]. There have been attempts to built scaffolds for islets transplantation that could solve problems of lack of ECM after isolation [29]. It has been proved by Authors of this proposal and other team independently, that islets encapsulated in special hydrogels could be used as a "bioink" in 3D bio-fabrication [29-30]. Nevertheless there are several weak points to be solved if one wants to achieve a 3Dprinted scaffold with pancreatic islets, which will be ready for transplantation (and with islets responding to glucose stimulus). To print islets they have to be immersed in some kind of gel, which will have a viscosity that allows of 3D printing but on the others hand glucose will be able to easily go through the matrix material. This situation only will allow islets to response properly for glucose stimuli. So far bioengineered hydrogels like alginate, polyglicane and many others allow to print islets and allow to keep them alive but function of this islets are limited [29]. Another problem that should be solved is the lack of vasculature. All attempts are being done with islets suspended in the hydrogel, suggesting that after transplantation, the vasculature will ingrow into the islets somehow. Unfortunately by the time the vasculature in-grows into the islets, most of them are already dead, because of lack of proper nutrition. The only answer for that problem might be engineering scaffold with vasculature in it and with using proper ECM for bioprinting. It is not an easy

task, but it seems that lately there has been a small breakthrough. Researchers managed to 3D - bioprint vessels with diameter of 0,5 mm diameter, which were physiologically active - nutrients and oxygen were possible to be transported through the wall and cells of endothelium of that vessels produced steady junction between them [31]. Such vessels would be appropriate for islets nutrition within printed scaffolds. Improving of 3D bioprinting technology might help to build scaffolds that will be able to be used in clinical medicine. Of the most importance seems to be engineering an Human Bionic Pancreas with islets and extracellular matrix which could help become an islet transplantation a method of treatment for definitely larger group of patients with diabetes then it is now. Implementation of such Bionic pancreas could lower costs paid on the treatment of diabetes mellitus and its complication and may reverse negative trends which says that diabetes will be one of the most common cause of death by the end of 2030 [2]. Results of that programme will give definitely a great progress in prevention of diabetic complications and help in treatment.

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