Austin Journal of Otolaryngology

Open Access

Austin Publishing Group

Research Article

Personalized Medicine in the Otorhinolaryngology

Coskunpinar E[1]*, Atici SZ[2], Hayretdag Ors C[3], Gorken B[2], Kurtaran H[2], Kosif HR[2], Dundar[2] and Enver N[4]

[1]Department of Medical Biology, Faculty of Medicine, University of Health Sciences, Istanbul, Turkey

[2]Faculty of Medicine, University of Health Sciences, Istanbul, Turkey

[3]Department of Anatomy, Faculty of Medicine, University of Health Sciences, Istanbul, Turkey

[4]Departments of Otorhinolaryngology and Head and Neck Surgery, Marmara University, Istanbul, Turkey

***Corresponding author:** Coskunpinar E, Department of Medical Biology, Faculty of Medicine, University of Health Sciences, Istanbul, Turkey

Received: April 10, 2018; **Accepted:** May 09, 2018; **Published:** May 16, 2018

Abstract

Personalized medicine in the otorhinolaryngology field especially can be used in implant construction, treatment and diagnosis by 3D-printers and stem cells. When there is a bone deformation in the jaw tumors, the fibula bone is taken with the veins and nerves and joined with the vessel in the neck, the bone is broken and shaped and given the final shape with the plate. Instead of this application, it is possible to replace the diseased bone removed with 3D bio-printing by copying the healthy jawbone and creating the exact same. The biocompatible material used has both less harmful effects and is more practical. Instead of prostheses in hearing loss, the cochlear stem cells can be developed as hear cells, which can lead to scientific and clinical progress in improving hearing loss. Stanford scientists have demonstrated that non-neural, preplacodal, otic-placode-like epithelia can be generated by using the gradual differentiation of the inner ear sensory epithelium from mouse embryonic cells in three-dimensional cell culture. It is also anticipated that in the near future tympanic membrane can be produced from the stem cells. It is now possible to apply personalized medicine to the test-positive areas that are made by biopsy instead of similar applications.

Keywords: Personalized Medicine; 3D Bio-Printing; Stem Cells; Otorhinolaryngology

Abbreviations

3D; HNSCC; 2D; NIH; ESC; CT; TME; TMJ; miPSC

Introduction

About precision medicine

The different treatment for each patient is requested for a long time but facilities were not sufficient. Now with the Human Genome Project it became the main focus of the developments. In the field of medicine, all these progressions opened a new area like precision medicine because of different influences after the treatments in people who have the same disease. Precision medicine is an approach that related with patient's genes, environment, and lifestyle and also interested in backgrounds of family features. All these subjects give us to decide which treatment can be use and which way is facilitate to get best results. Precision medicine is not discovered in a few years. It's benefits always known for years. For example blood transfusion has a precision approach [1]. Precision medicine aims to predict the disease, reduce the rate of side effects of drugs, and provide drugs with genomic knowledge, in short think of each patient differently. In the future, precision medicine gives lots of chance to treat people and provides to get precaution for early diagnosis.

Biomarkers in HNSCC

Head and neck squamous cell carcinoma (HNSCC), which includes cancers of the oral cavity, larynx, pharynx, salivary glands, and nose/nasal passages, is one of the predominant causes of cancer related casualties worldwide [2]. Overall prognosis in HNSCC has improved to some extent with the advancements in therapeutic modalities but detection of primary tumor at its initial stage and prevention of relapse are the major targets to be achieved for further improvement in terms of survival rate of patients [3]. With biomarkers, biological molecules that act as indicators of a chemical process in body fluids or tissues [4], early recognition of HNSCC is much more possible.

3D Printing in Medicine

Three-dimensionally (3D) printing is an emerging technique in medicine. Printing form is designed using computer aided design (CAD) software. The 3D design is then passed to a slicing program that parses the solid object into a stack of thin, axial cross sections. The sections are then sent to the printer, and each respective 2D cross section is reproduced in order, starting from the bottom and printing up along the Z axis [5]. National Institutes of Health (NIH) launched the NIH 3D print exchange, an online portal for accurate, reliable and informative 3D models for researchers and educators. With this portal, users have the ability to create pre-printable 3D files from molecular structure data, microscopic image stacks and computer tomography scan data [6]. The pharmaceutical field is approved by the US Food and Drug Administration for the first 3D printed tablets in 2015 [7].

Stem Cells and Otorhinolaryngology

Stem cells have a remarkable potential to transform into many different cell types during early life and growth. In addition, stem cells function as a kind of internal repair system that is divided without limitation to regenerate other cells. If a stem cell divides, each new cell has the potential to become either a stem cell or another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. Regenerate they through cell division can be induced to become tissue or organ specific cells with specific functions under certain physiological or experimental conditions [8]. Nowadays the production of personalized tissue with stem cells is becoming widespread.

Citation: Coskunpinar E, Atici SZ, Hayretdag Ors C, Gorken B, Kurtaran H, Kosif HR, et al. Personalized Medicine in the Otorhinolaryngology. Austin J Otolaryngol. 2018; 5(1): 1101.

Material and Method

Medical applications in 3d printing

When there is a bone deformation in the jaw tumors, the fibular bone is taken with the veins and nerves and joined with the vessel in the neck, the bone is broken and shaped and given the final shape with the plate. Instead of this application, it is possible to replace the diseased bone removed with 3D bio-printing by copying the healthy jawbone and creating the exact same. Digital datasets of the patient's jaws and wax trial in occlusion are used to segment the bone and dental arches, for the design of a sub-periosteal frame and abutments in the optimal location related to the dental arch and for the design of the superstructure. The implants and superstructure are 3D printed in titanium alloy [9,10]. The biocompatible material used has both less harmful effects and is more practical.

Stem cells and tissue production

Instead of prostheses in hearing loss, the cochlear stem cells can be developed as hearing cells, which can lead to scientific and clinical progress in improving hearing loss. Stanford scientists have demonstrated that non-neural, preplacodal, and otic-placode-like epithelia can be generated by exploiting the gradual differentiation of the inner ear sensory epithelium from mouse embryonic cells in three-dimensional culture [11]. It is also anticipated that in the near future tympanic membrane can be produced from the stem cells. Scientists report the stepwise differentiation of inner ear sensory epithelia from mouse embryonic stem cells (ESCs) in three-dimensional culture. They show that ESC aggregates transform sequentially into non-neural, preplacodal and otic-placode-like epithelia. These stem-cell-derived hair cells exhibit functional properties of native mechanosensitive hair cells and form specialized synapses with sensory neurons that have also arisen from ESCs in the culture. Thus, inner ear differentiation model was created [12].

Biomarkers

It is now possible to apply precision medicine to the test-positive areas that are made by biopsy instead of similar applications that are made in the field of oncology. Today, we can remove the disease with medication and surgical intervention in the treatment of cancer, but the main problem is to prevent cancerous repetition. The cancerous area after the surgical intervention can be removed but there are cells that are not cancerous but are able to become cancerous around this region. Since these cells cannot be detected molecularly during surgery, it is possible that the cancer recovers after intervention. More precise intervention can be performed using the appropriate biomarker.

Results

According to a case study published in the New England Journal of Medicine tracheal splint that produced by using 3D printer and computer tomography (CT) images, was surgically implanted in a baby with tracheobronchomalacia and the operation was successful [13,14].

With a new technique that called malbourne, prosthesis was developed for a 58-year-old female recipient of TME's last stage osteoarthritis. The load response of the prosthesis during chewing and a maximum-force bite was quantified using a personalized musculoskeletal model of the patient's masticatory system developed using medical images. The prosthesis fabricated using 3D printing. Six months post-operatively, the prosthesis recipient had a normal jaw opening distance, with no complications identified. The new design features and immediate load response of the Melbourne prosthetic TMJ suggests that it may provide improved clinical and biomechanical joint function and reduce risk of intra-operative nerve damage during placement [15].

In a study the application of 3D print technique in reconstruction of complex jaw defect after removal of maxillofacial cancer evaluated from May 2013 to January 2015, 10 cases were enrolled in the study, 3 were maxillary defects and 7 were mandibular defects. Preoperative computer-aided design and modeling with 3D printer, intraoperative ablation and fibula formation according to template, flap suture and vascular anastomosis were performed. All the cases were successfully operated according to preoperative computer aided design, and all the fibulas and skin islands survived. All the cases had regular diet 2 weeks after surgery and showed satisfying appearance. Digital and 3D print technique has good practicability in reconstruction of complex jaw defect with free fibula [16].

Patient informed by modeling with 3D printer makes patient better understand the intervention process and patient satisfaction increases. The results were successful and patient satisfaction increased [17]. It has been determined that Precision Medicine has achieved success with its precision measurement capability supported by 3D printer technology and the use of biocompatible materials [9,10].

Results of stem cell applications

As an example of stem cell studies, scientists transplanted naive mouse-derived induced pluripotent stem cells (miPSCs) into the otocysts of wild type mice at embryonic day 11.5. The transplanted miPSCs survived in the lumens of the inner ears at E13.5 and E15.5 in wild type mice. Results suggest that otocyst transplanted cells survived and differentiated. These findings may offer some hope for cell transplantation therapy for profound genetic hearing loss [18].

Discussion

If we consider the quantitative measurement sensitivity of technology, we can see how much 3D printer can do for the precision medicine. The variation of intervention is necessary for some patients but traditional interventions can be insufficient. The required sensitive measurement can be provided by the technology. It also allows us to get quick results. The measurement reliability makes it easier to scan and remove the mold. We can predict the result of the designed intervention. Another benefit of modelling with 3D printer issuing the artificial models instead of using animals can be time-saving and less animal damage. Increasingly affordable three-dimensional (3D) printing technologies now make it possible for surgeons to create highly customizable patient-tailored products. The 3D printing provides the ability to construct complex individualized implants that not only improve patient outcomes but also increase economic feasibility. The technology offers a potential level of accessibility that is paramount for remote and resource-limited locations where health care is most often limited. The 3D printing-based technologies will have an immense impact on the reconstruction of traumatic injuries,

facial and limb prosthetic development, as well as advancements in biologic and synthetic implants. Before the preparation, the relevant region is scanned and the model with correct anatomical shape is formed with the 3D printer. With this model, the patient intervenes and the complications that may arise are explained. The understanding and satisfaction of the patients who are informed by this method are increased at high rate [17]. With the falling price, it is possible that 3D printers will be so widespread in the near future that perhaps one can be found at each hospital.

Today, medicines are guaranteed according to the success rate in the tested groups, but when the personalized drug is made, the patient is the first to experience it. How can the reliability of these drugs be tested? We think, it is possible to get fast results by printing with medicine design 3D printer in making personalized drug. For the test phase, the tissue that drug will be effect can print in three-dimension by using patient's cells. By doing so, we will be able to apply fast, reliable and harmless precision medicine. Published applications also support this idea. Biomarkers enable us to understand the pathology of the disease better, evaluate the response to the treatment, determine which drug the patient will receive and in what dose, and monitor the prognosis of the healing. Early detection of head and neck squamous cell carcinoma is vital in improving the overall survival and prognosis. It can be achieved by use of latest biomarkers. With advancement in knowledge of molecular characteristics of this disease, various biomarkers acting at molecular level have been identified [2].

References

1. Head and Neck Patient Version.
2. What is the precision medicine? NIH.
3. Dahiya K, Dhankhar R. Updated overview of current biomarkers in head and neck carcinoma. World J Methodol. 2016; 6: 77-86.
4. Parisa Sharafi. Hacettepe University Faculty of Medicine Department of Medical Biology, Ankara/ Turkey. Hacettepe Medical Journal. 2010; 41: 142-146.
5. O'Brien CM, Holmes B, Faucett S, Zhang LG. Three-Dimensional Printing of Nanomaterial Scaffolds for Complex Tissue Regeneration. Tissue Engineering. Part B, Reviews 2015; 21: 103-114.
6. Coakley MF, Hurt DE, Weber N, Mtingwa M, Fincher EC, Alekseyev V, et al. The NIH 3D Print Exchange: A Public Resource for Bioscientific and Biomedical 3D Prints. 3D Print Addit Manuf. 2014; 1: 137-140.
7. Tagami T, Fukushige K, Ogawa E, Hayashi N, Ozeki T. 3D Printing Factors Important for the Fabrication of Polyvinylalcohol Filament-Based Tablets. Biol Pharm Bull. 2017; 40: 357-364.
8. NIH Stem Cell Information Home Page. In Stem Cell Information [World Wide Web site]. Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services. 2016.
9. Mommaerts MY. Additively manufactured sub-periosteal jaw implants. Int J Oral Maxillofac Surg. 2017; 46: 938-940.
10. Jeon B, Lee C, Kim M, Choi TH, Kim S, Kim S. Fabrication of three-dimensional scan-to-print ear model for microtia reconstruction. J Surg Res. 2016; 206: 490-497.
11. Jackler RK. A regenerative method of tympanic membrane repair could be the greatest advance in otology since the cochlear implant. Otol Neurotol. 2012; 33: 289.
12. Koehler KR, Mikosz AM, Molosh AI, Patel D, Hashino E. Generation of inner ear sensory epithelia from pluripotent stem cells in 3D culture. Nature. 2013; 500: 217-221.
13. Ventola CL. Medical Applications for 3D Printing: Current and Projected Uses. P T. 2014; 39: 704-711.
14. Bartlett S. Printing organs on demand. Lancet Respir Med. 2013; 1: 684.
15. Ackland DC, Robinson D, Redhead M, Lee PV, Moskaljuk A, Dimitroulis G. A personalized 3D-printed prosthetic joint replacement for the humantemporomandibular joint: From implant design to implantation. J Mech Behav Biomed Mater. 2017; 69: 404-411.
16. Liu J, Zhang B, Yan D, Yu X, Lin M, Li Z, et al. Digital and three-demention print technique in reconstruction for complex defect after resection of jaw neoplasms. 2015; 50: 473-476.
17. Atalay HA, Canat HL, Ülker V, Alkan İ, Özkuvanci Ü, Altunrende F. Impact of personalized three-dimensional (3D) printed pelvicalyceal system models on patient information in percutaneous nephrolithotripsy surgery: A pilot study. Int Braz J Urol. 2017; 43: 470-475.
18. Takeda H, Minoda R, Miwa T, Yamada T, Ise M. Transplanting mouse induced pluripotent stem cells into mouse otocysts *in vivo*. Neurosci Lett. 2017; 647: 153-158.

Citation: Coskunpinar E, Atici SZ, Hayretdag Ors C, Gorken B, Kurtaran H, Kosif HR, et al. Personalized Medicine in the Otorhinolaryngology. Austin J Otolaryngol. 2018; 5(1): 1101.