March 15, 2019

Dear Regina,

Welcome to BioMarketing Insight's monthly newsletter.

Last month, I covered "Thinking Outside the Box in Fighting Cancer." If you missed last month's article, click here to read it. This month we'll cover "3D Printing - Where Are We Today?"

Read on to learn more about this topic and other current news. The next newsletter will be published on April 15th, 2019.

We encourage you to share this newsletter with your colleagues by using the social media icons below, or by simply forwarding this newsletter or use the link below. Should you or your colleagues want to join my mailing list, click on the link below.

Sincerely,
Regina Au
Principal, New Product Planning/
Strategic Planning Consultant
BioMarketing Insight

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Developing a Product? Commercializing a Product?

If you are developing a product and have not conducted the business due diligence to determine commercial viability or success, contact me for an appointment. For successful commercial adoption of your product or looking to grow your business, contact me for an appointment.

For more information on our services, click on the links below:

Product Development
Market Development
Marketing Strategies

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I am pleased to announce that my article entitled "Updates in Solving the Mystery of Alzheimer's Disease Pathology" was published in the International Journal of Clinical Pharmacology & Pharmacotherapy. This commentary reviews the "Updated Proposed timeline of biomarker abnormalities leading to cognitive impairment" and the involvement of both beta amyloid clearance and plaque, and tau clearance and tau-mediated neuronal injury and dysfunction. To read the article, click here.

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Why Our Microbiome is Important to Our Physiology and Diseases

I am pleased to announce that my article entitled "Why Our Microbiome is Important to Our Physiology and Diseases" was published in the International Journal of Clinical Pharmacology & Pharmacotherapy. This article reviews the results of the Human Microbiome Project and the factors that affect our microbiome in relation to our healthy state and dysbiosis or disease state. To read the article, click here.

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Immunooncology: Can the Right Chimeric Antigen Receptors T-Cell Design Be Made to Cure All Types of Cancers and Will It Be Covered?

I am pleased to announce that my article on "Immunooncology: Can the Right Chimeric Antigen Receptors T-Cell (CAR-T) Design Be Made to Cure All Types of Cancers and Will It Be Covered?" has been published in Journal of Pharmaceutics. This article reviews the mechanism, design and administration of CAR-T cells, and whether payers will pay for this new technology. To read the article, click here.

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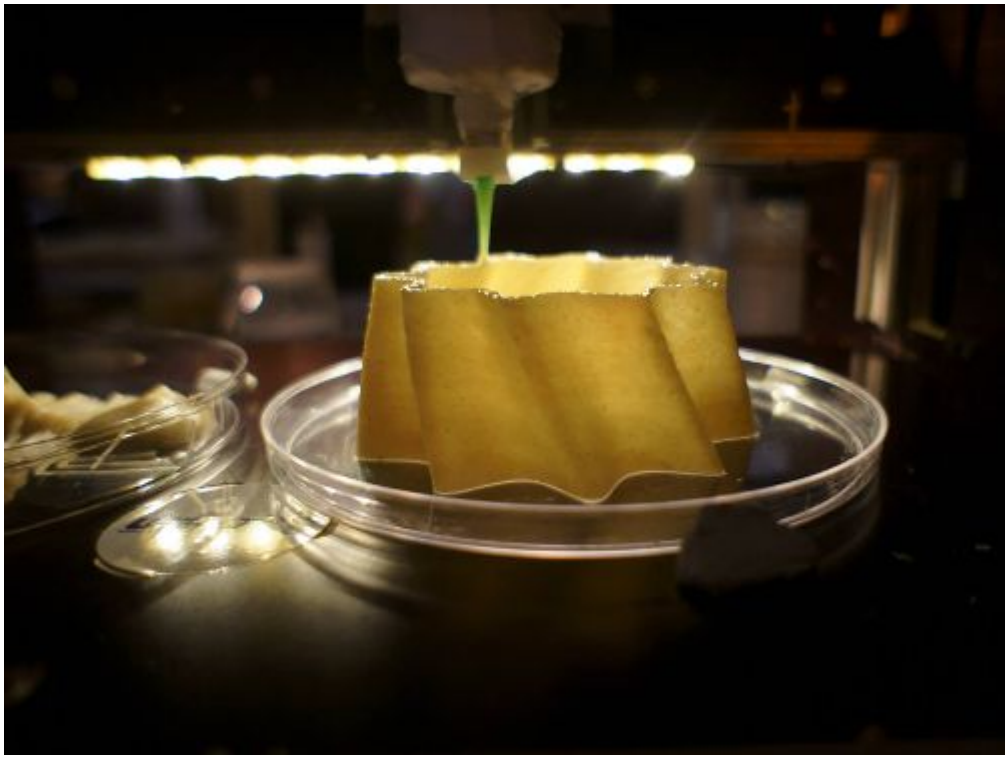
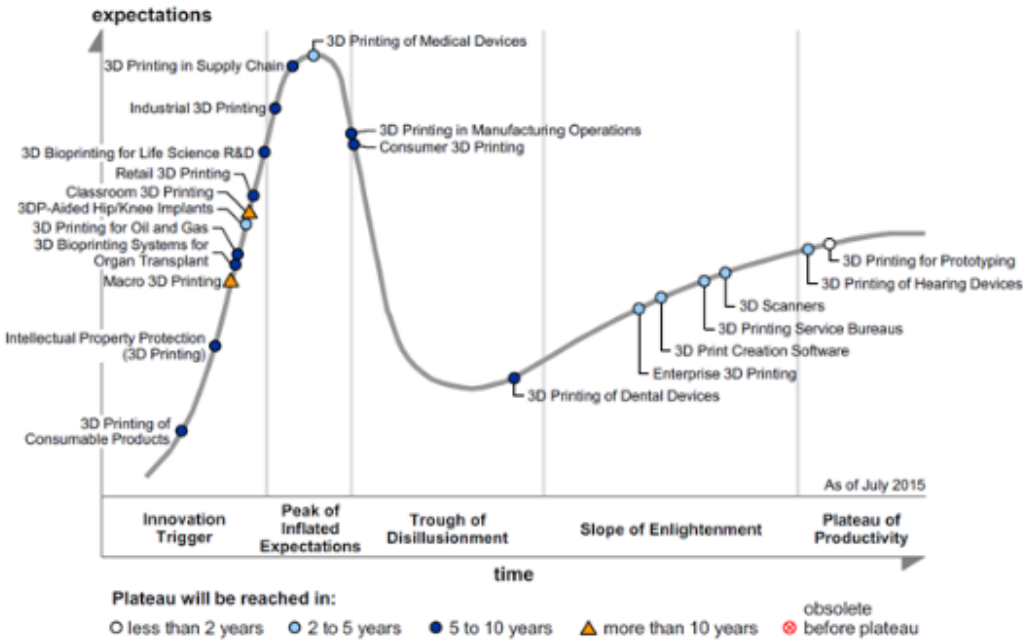


3D Printing - Where Are We Today?

using 3D printing for practically everything. People were exciting because it was new and there were endless possibilities.

However, Gartner classifies this as the "Hype Cycle" (see graph 1) where everyone started using it for all sorts of applications because it was novel. But when one investigates further, it may not have been everything people thought it could accomplish for many reason and here are a few: 1) it may not be cost effective compared to mass production; 2) there may not be a big enough market for a particular application, 3) it may interrupt the normal work flow; or 4) it may not be as good as the traditional method of reproducing the product. This is what one call the "Trough of Disillusionment". And through lessons learned, people focus on 3D printing where it works and is beneficial.



Graph 1: Gartner's 3D printing hype cycle curve from 2017.
Source: fabbaloo.com/blog

For the medical field, 3D Printing took off in the medical device world because one could customize devices to each patient, much like personalized medicine. There are the four main areas that have pushed innovation with 3D printing: 1) prosthetics; 2) wearables and implants; 3) surgical planning; and 4) bioprinting. Examples of each to follow.

How is 3D printing accomplished in the medical device world? 3D printers can use almost any type of material that can be in a liquefied state including stem cells or living cells. The printer is similar to an inkjet printer but more sophisticated and the product is built layer by layer until one has a 3D replica. In order to form the 3D replica, the object is either scanned or designed using a software program call Computer-Aided Design or CAD.

examples of 3D designed and printed prosthetics (Image 1 & 2)

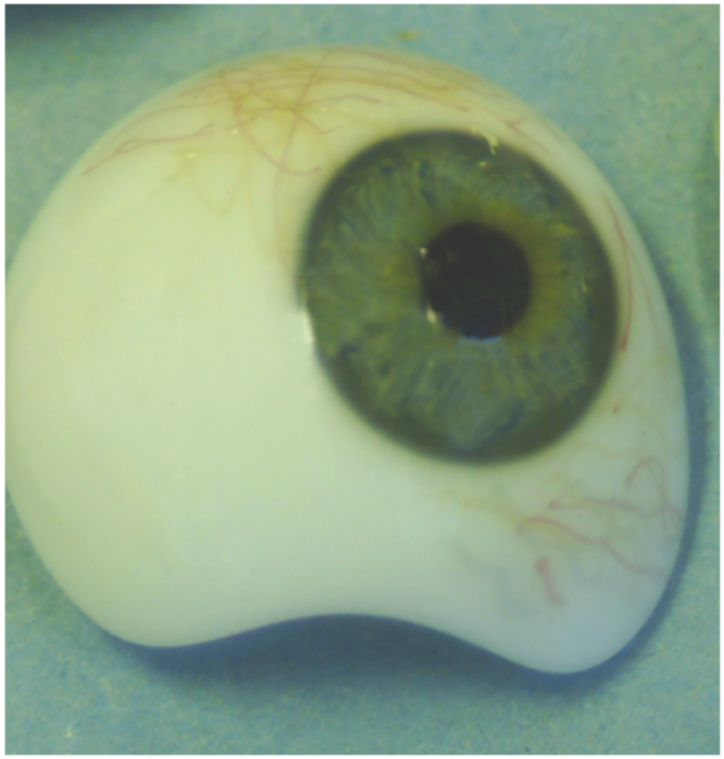


Image 1: 3D printed eye
Source: *Image: Liz Gill, Manchester Metropolitan University, UK*

Image 2: 3D printed ear probably made from collagen and then painted to give it an life-like appearance.
Source: 3D Spectra Tech

1) Cost - a conventional commercial-made prosthetics can cost between $5,000 and $50,000 which meant unless one has very good insurance or money is no object, majority of the people can't afford to get a prosthesis.

2) Speed - a 3D printed prosthesis can be make in one day as oppose to weeks or months to produce and calibrate regular prosthetic limbs.

3) Versatility - 3D prosthetics can be customized to each individual and their activities at a reasonable cost verses conventional prosthesis that could cost a fortune for customization.

4) Growth - particularly for children who grow out of their prosthesis quickly, one can just print another one. It's a burden on the family to pay out $10,000 or so every year, or every other year for commercial-made prosthetics.

5) Comfort - because these prosthesis are custom made to the individual, they would fit like a glove and are comfortable.

II) **Wearables and Implants**- 3D printing is perfect for wearables and implants since it can be customized to each individual patient to correct a medical issue and it's comfortable because it fits perfectly. These products usually have to be sturdy but light weight at the same time to ensure it's comfortable (see Image 3 & 4).

Image 3: Wearable - Scoliosis brace to correct the spine
Source: 3dprint.com

Image 4: Implant- this 3D printed spine functions and looks exactly like the traditional implant
Source: https://www.mirror.co.uk

III) **Surgical Planning** - 3D anatomy models of the body such as the heart, brain, and leg has greatly enhanced surgical procedures and reduced surgical risk. A surgeon can now print out for example the brain of the patient's specific anatomy or defect from their MRI, PET or CT image and plan his/her surgical procedure (see Image 5). This allows a surgeon to prepare for what was once unanticipated problems because sometimes a surgeon won't know what s/he will encounter until s/he opens the patient.

By conducting this pre-planning procedure, it reduces risk and it shortens the procedure time. There is always a risk the longer the patient is under anesthesia during surgery and possible post operative issues from the affects of being under anesthesia too long.

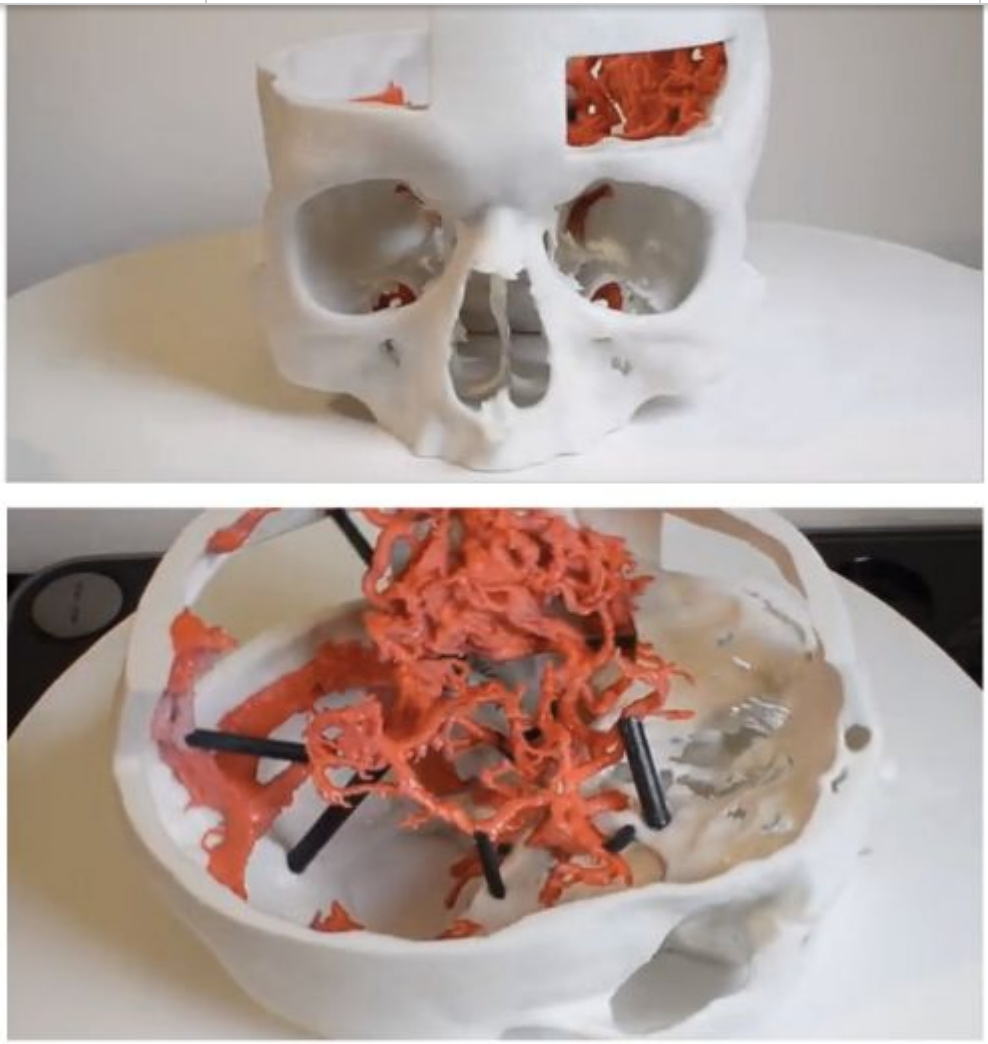


Figure 5 A 3D model used for surgical planning by neurosurgeons at the Walter Reed National Military Medical Center.[12]

IV) **Bioprinting**- This process involves living cells such as stem cells. Pluripotent or undifferentiated stems cells can be programmed or induced into various organ such as the kidney, blood vessels and liver. Using these iPS (induced Pluripotent Stem) cells scientist are working vigorously to be able to print a fully function 3D organ for organ transplant and drug testing since there is a shortage of organ donors and to eliminate using animals for drug testing (Images 6, 8 & 9).

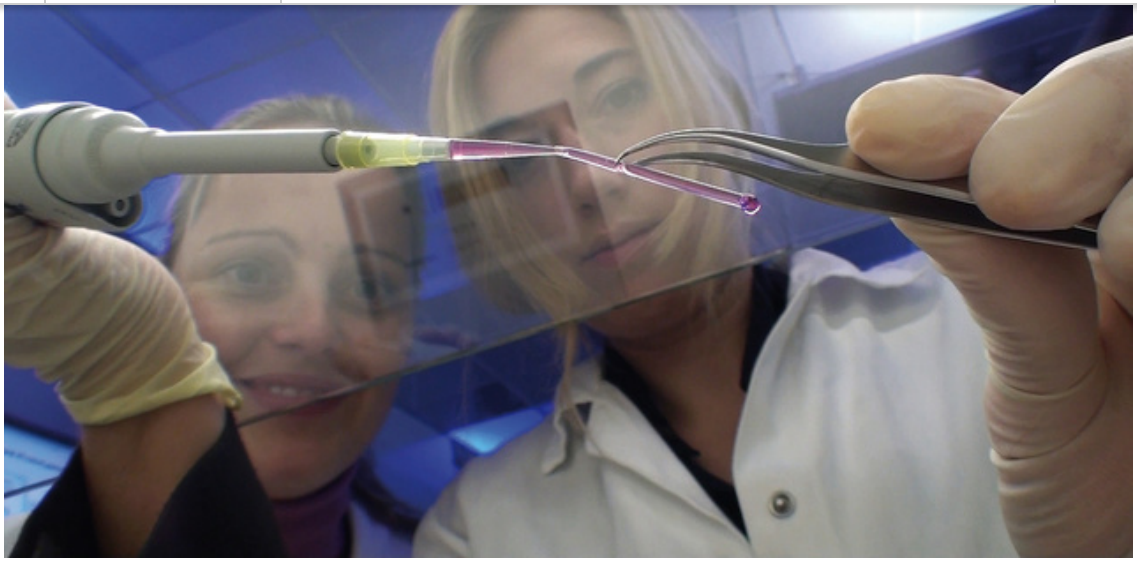


Image 6: Printed living blood vessels
Source: Fraunhofer Institute for Interfacial Engineering and Biotechnology.

Printing blood vessels are harder, because one needs to create a functioning circulatory system to go with it stated Gunter Tovar, a German scientist who heads up the Fraunhofer Institute for Interfacial Engineering and Biotechnology.

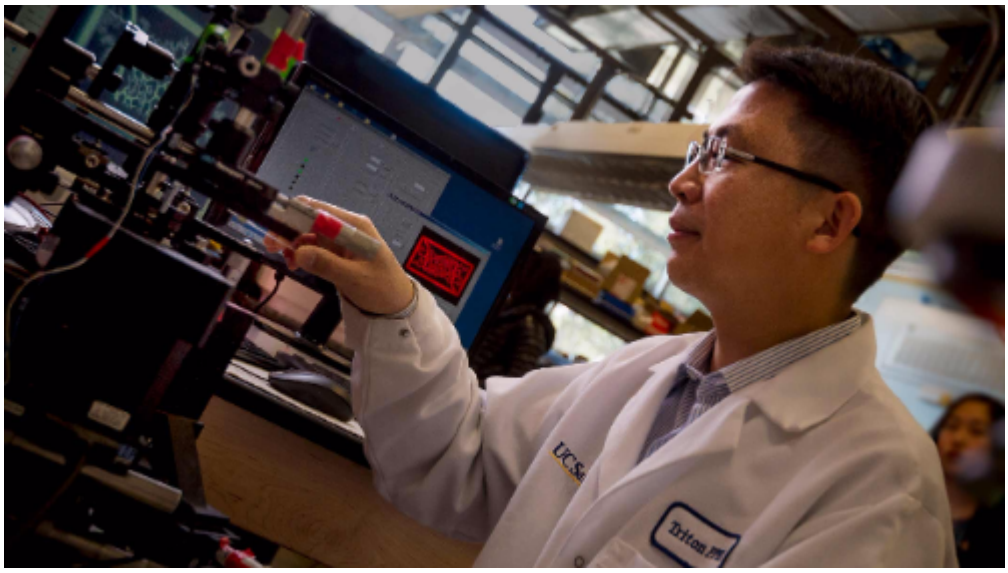


Image 7: Shaochen Chen, a nanoengineer professor from Univ. of California, San Diego.
Source: Chen's Lab, Univ. of CA, San Diego

Professor Shaochen Chen, stated that one of the biggest challenges in tissue engineering is to create lifelike tissues and organs with functioning vasculature; networks of blood vessels that can transport blood, nutrients, waste and other biological materials and do it safely when implanted inside the body.

taken a big step toward that goal."

Chen's lab has been able to print a 3D vasculature network that can be safely integrated with the body's own network to circulate blood. These blood vessels branch out into many series of smaller vessels, similar to the blood vessel structures found in the body. The goal is to rapidly produce intricate 3D microstructures that mimic the sophisticated designs and functions of biological tissues.

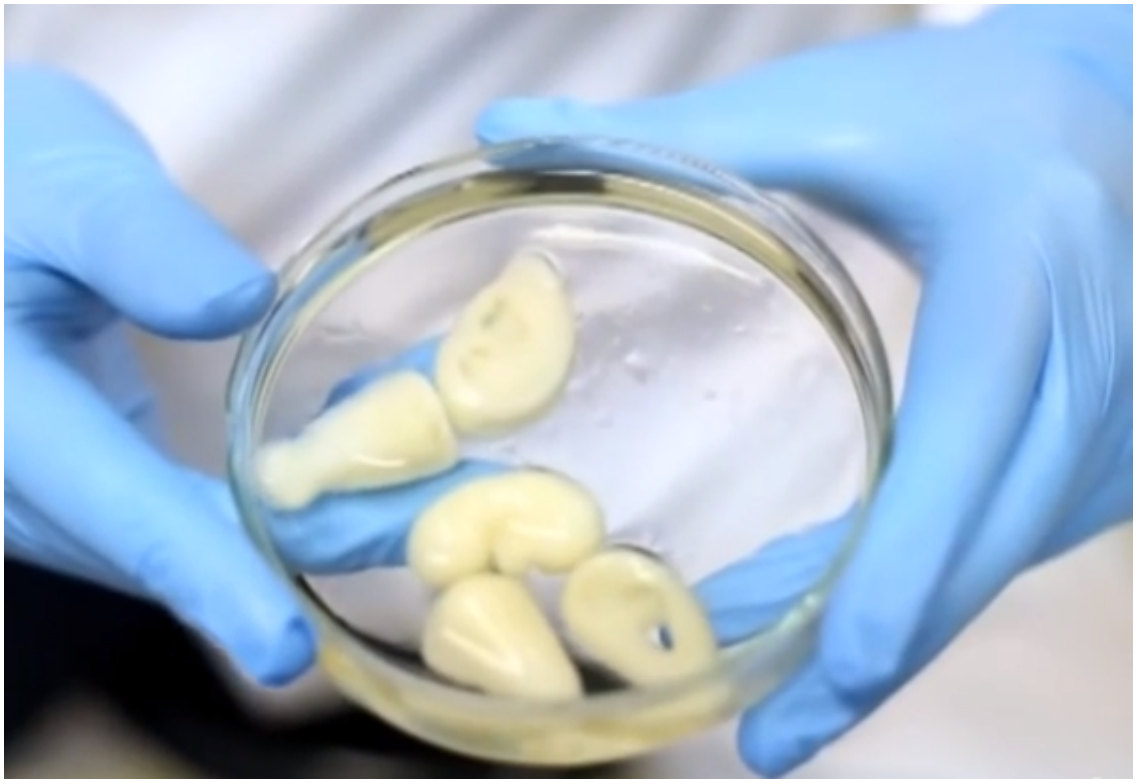


Image 8: 3D Printed living kidneys
Source: *Image: Professor Xu, Hangzhou Normal University, China*

Professor Xu Mingen from Hangzhou Normal University: School of Medicine in Zhejiang Province has been able to print mini 3D living kidney. The 3D kidney can function like a human kidney in terms of breaking down toxins and metabolites and can live up to 4 hours. The ultimate goal is to use a 3D printed kidney from a patient's own cell for organ transplant and decrease the risk of organ rejection.

Image 9: Printed living liver tissues
Source: CBS news and Organovo

Organovo, a San Diego-based company has been able to print samples of liver cells that function as they would in a human. Their researchers used a gel to build three types of liver cells and arranged them in a three-dimensional cell architecture normally found in a human liver. Although these 3D cells are not fully functional, they are able to produce some of the same proteins as a human liver and interact with other compounds that the cells would normally come into contact in the body.

The company is hoping to use these printed liver cells or tissue to test drugs or investigate the effect of certain diseases.

Concerns

While 3D Printing has made great strides in the medical field particularly when it comes to personalized medicine, like everything else there are pro's and con's. Here are some of the main concerns that still need to be answered should hospitals, medical centers and physicians decide to incorporate 3D printing into their practice:

1. Regulatory Oversight
    a. No structured framework - for hospitals, medical centers and physicians
2. Reimbursement - will all insurance companies pay and how much for these device including bioprinting?
3. Cost of Printers - to have one for every physician's practice or more for every department in the hospital?
4. Patent Infringement - on the device itself?
5. Biocompatibility - will all materials be biocompatible with each patient? Should there be testing before use?
6. Trained experts - does one need to be trained to ensure quality and durability?

Most of these issues can be solved if medical centers, hospitals and physicians use 3D printing medical device vendors instead of trying to print the device themselves. The only

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Closing Thoughts

The application of 3D printing for personalize medicine (Gartner predicted that medical device applications would plateau in 2-5 years) will continue to grow and expand into other medical area that I did not mention such as dentistry, hearing devices and possibly devices applicable to the geriatric population which is growing.

Bioprinting of fully functional organs that would last for years however will take a while to materialize for organ transplant. But this field has already made great strides in being able to print a mini functional or partially functional organ or blood vessel network in such a short period of time. Using printed organ cells has already begun for drug testing and to investigate the effects of certain disease on these tissues will help advance the understanding of disease tremendously.

For personalize medicine application, the sky is the limit. It's a matter of whether the application makes business and regulatory sense.

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Should you have any questions or need of assistance with your business due