

Student Name:	
Matriculation Number:	
Date:	

Section	Time	% of grade	Grade:
Listening Comprehension	30 min	25	
Reading Comprehension	60 min	25	
Case Study: Background & Writing	105 min	25	
Case Study: Speaking	30 min	25	
		Total Grade:	

1st Examiner:

2nd Examiner:



Part 1: Listening Comprehension

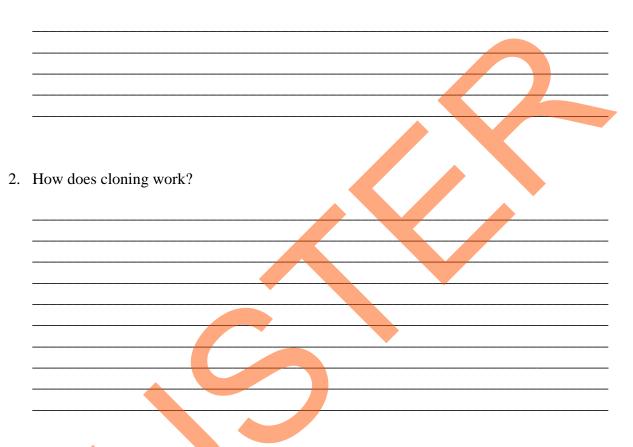
The audio will introduce the topic of this exam: Cloning and 3D Bioprinting

Listen to the audio clip and take notes in the space provided below. Your notes will not be graded. Then read the comprehension questions and listen to the audio clip once more. Answer the associated comprehension questions in paragraph form using complete sentences. Please take notes only in this examination booklet. Your notes will not be graded. You will have 30 minutes to complete this section of the test which covers 25% of the overall exam grade.

Audio:	What is human cloning, and is it possible? (YouTube video)
Notes:	

Listening Comprehension Questions

1. What analogy does he use to explain what a clone is, and what is exactly the same in both the clone and its donor?



3. Describe what you think he means when he speaks of the process as "human cloning as an interventive activity" compared to "in the identical twin sort of way".



4. In which way is a cloned copy not identical to its donor?

5. In order from best to worst, list the living organisms mentioned in the video that are able to clone. Inferring from what he's explained in the video, why are these organisms in this particular order?



Part 2: Reading Comprehension

The article will develop the topic of this exam: Cloning and 3D Bioprinting

Read the article. Then answer the associated comprehension questions using full, complete sentences. Please take notes only in this examination booklet. Your notes will not be graded. You will have 60 min to complete this section of the test which covers 25% of the overall exam grade.

Article: Medical Applications for 3D Printing: Current and Projected Uses

Notes:

Medical Applications for 3D Printing: Current and Projected Uses

by C. Lee Ventola, MS (2014)

WHAT IS 3D PRINTING?

Three-dimensional (3D) printing is a manufacturing method in which objects are made by fusing or depositing materials—such as plastic, metal, ceramics, powders, liquids, or even living cells—in layers to produce a 3D object.^{1,8,9} This process is also referred to as additive manufacturing (AM), rapid prototyping (RP), or solid free-form technology (SFF).⁶ Some 3D printers are similar to traditional inkjet printers; however, the end product differs in that a 3D object is produced.¹ 3D printing is expected to revolutionize medicine and other fields, not unlike the way the printing press transformed publishing.¹

There are about two dozen 3D printing processes, which use varying printer technologies, speeds, and resolutions, and hundreds of materials.⁹ These technologies can build a 3D object in almost any shape imaginable as defined in a computer-aided design (CAD) file.⁹ In a basic setup, the 3D printer first follows the instructions in the CAD file to build the foundation for the object, moving the printhead along the x–y plane.⁵ The printer then continues to follow the instructions, moving the printhead along the z-axis to build the object vertically layer by layer.⁵ It is important to note that two-dimensional (2D) radiographic images, such as x-rays, magnetic resonance imaging (MRI), or computerized tomography (CT) scans, can be converted to digital 3D print files, allowing the creation of complex, customized anatomical and medical structures.^{3,5,10}

OVERVIEW OF CURRENT APPLICATIONS

Commercial Uses

3D printing has been used by the manufacturing industry for decades, primarily to produce product prototypes.^{1,9} Many manufacturers use large, fast 3D printers called "rapid prototyping machines" to create models and molds.¹¹ A large number of .stl files are available for commercial purposes.¹ Many of these printed objects are comparable to traditionally manufactured items.¹

Companies that use 3D printing for commercial medical applications have also emerged.² These include: Helisys, Ultimateker, and Organovo, a company that uses 3D printing to fabricate living human tissue.² At present, however, the impact of 3D printing in medicine remains small.¹ 3D printing is currently a \$700 million industry, with only \$11 million (1.6%) invested in medical

applications.¹ In the next 10 years, however, 3D printing is expected to grow into an \$8.9 billion industry, with \$1.9 billion (21%) projected to be spent on medical applications.¹

Consumer Uses

3D printing technology is rapidly becoming easy and inexpensive enough to be used by consumers.^{9,11} The accessibility of downloadable software from online repositories of 3D printing designs has proliferated, largely due to expanding applications and decreased cost.^{2,4,11} It is now possible to print anything, from guns, clothing, and car parts to designer jewelry.² Thousands of premade designs for 3D items are available for download, many of them for free.¹¹

This low-cost hardware and growing interest from hobbyists has spurred rapid growth in the consumer 3D printer market.¹¹ A relatively sophisticated 3D printer costs about \$2,500 to \$3,000, and simpler models can be purchased for as little as \$300 to \$400.^{8,11} For consumers who have difficulty printing 3D models themselves, several popular 3D printing services have emerged, such as Shapeways, (<u>www.shapeways.com</u>), Thingiverse (<u>www.thingiverse.com</u>), MyMiniFactory (<u>www.myminifactory.com</u>), and Threeding (<u>www.threeding.com</u>).¹¹

BENEFITS OF 3D PRINTING IN MEDICAL APPLICATIONS

Customization and Personalization

The greatest advantage that 3D printers provide in medical applications is the freedom to produce custom-made medical products and equipment.³ For example, the use of 3D printing to customize prosthetics and implants can provide great value for both patients and physicians.³ In addition, 3D printing can produce made-to-order jigs and fixtures for use in operating rooms.⁴ Custom-made implants, fixtures, and surgical tools can have a positive impact in terms of the time required for surgery, patient recovery time, and the success of the surgery or implant.⁴ It is also anticipated that 3D printing technologies will eventually allow drug dosage forms, release profiles, and dispensing to be customized for each patient.⁵

Increased Cost Efficiency

Another important benefit offered by 3D printing is the ability to produce items cheaply.¹ Traditional manufacturing methods remain less expensive for large-scale production; however, the cost of 3D printing is becoming more and more competitive for small production runs.¹ This is especially true for small-sized standard implants or prosthetics, such as those used for spinal, dental, or craniofacial disorders.³ The cost to custom-print a 3D object is minimal,

with the first item being as inexpensive as the last.¹ This is especially advantageous for companies that have low production volumes or that produce parts or products that are highly complex or require frequent modifications.⁴

3D printing can also reduce manufacturing costs by decreasing the use of unnecessary resources.⁵ For example, a pharmaceutical tablet weighing 10 mg could potentially be custom-fabricated on demand as a 1-mg tablet.⁵ Some drugs may also be printed in dosage forms that are easier and more cost-effective to deliver to patients.⁵

Enhanced Productivity

"Fast" in 3D printing means that a product can be made within several hours.⁴ That makes 3D printing technology much faster than traditional methods of making items such as prosthetics and implants, which require milling, forging, and a long delivery time.³ In addition to speed, other qualities, such as the resolution, accuracy, reliability, and repeatability of 3D printing technologies, are also improving.³

Democratization and Collaboration

Another beneficial feature offered by 3D printing is the democratization of the design and manufacturing of goods.⁴ An increasing array of materials is becoming available for use in 3D printing, and they are decreasing in cost.⁴ This allows more people, including those in medical fields, to use little more than a 3D printer and their imaginations to design and produce novel products for personal or commercial use.⁴

The nature of 3D printing data files also offers an unprecedented opportunity for sharing among researchers.⁶Rather than trying to reproduce parameters that are described in scientific journals, researchers can access downloadable .stl files that are available in open-source databases.⁶ By doing so, they can use a 3D printer to create an exact replica of a medical model or device, allowing the precise sharing of designs.⁶ Toward this end, the National Institutes of Health established the 3D Print Exchange (<u>3dprint.nih.gov</u>) in 2014 to promote open-source sharing of 3D print files for medical and anatomical models, custom labware, and replicas of proteins, viruses, and bacteria.¹²

MEDICAL APPLICATIONS FOR 3D PRINTING

3D printing has been applied in medicine since the early 2000s, when the technology was first used to make dental implants and custom prosthetics.^{6,10} Since then, the medical applications for 3D printing have evolved considerably. Recently published reviews describe the use of 3D printing to produce bones, ears, exoskeletons, windpipes, a jaw bone, eyeglasses, cell cultures,

stem cells, blood vessels, vascular networks, tissues, and organs, as well as novel dosage forms and drug delivery devices.^{1,3,11} The current medical uses of 3D printing can be organized into several broad categories: tissue and organ fabrication; creating prosthetics, implants, and anatomical models; and pharmaceutical research concerning drug discovery, delivery, and dosage forms.² A discussion of these medical applications follows.

Bioprinting Tissues and Organs

Tissue or organ failure due to aging, diseases, accidents, and birth defects is a critical medical problem.¹⁰Current treatment for organ failure relies mostly on organ transplants from living or deceased donors.¹⁰However, there is a chronic shortage of human organs available for transplant.^{1,10} In 2009, 154,324 patients in the U.S. were waiting for an organ.¹⁰ Only 27,996 of them (18%) received an organ transplant, and 8,863 (25 per day) died while on the waiting list.¹⁰ As of early 2014, approximately 120,000 people in the U.S. were awaiting an organ transplant.¹ Organ transplant surgery and follow-up is also expensive, costing more than \$300 billion in 2012.¹⁰ An additional problem is that organ transplantation involves the often difficult task of finding a donor who is a tissue match.¹ This problem could likely be eliminated by using cells taken from the organ transplant patient's own body to build a replacement organ.^{1,13} This would minimize the risk of tissue rejection, as well as the need to take lifelong immunosuppressants.^{1,13}

Although 3D bioprinting systems can be laser-based, inkjet-based, or extrusion-based, inkjetbased bioprinting is most common.¹³ This method deposits "bioink," droplets of living cells or biomaterials, onto a substrate according to digital instructions to reproduce human tissues or organs.¹³ Multiple printheads can be used to deposit different cell types (organ-specific, blood vessel, muscle cells), a necessary feature for fabricating whole heterocellular tissues and organs.¹³ A process for bioprinting organs has emerged: 1) create a blueprint of an organ with its vascular architecture; 2) generate a bioprinting process plan; 3) isolate stem cells; 4) differentiate the stem cells into organ-specific cells; 5) prepare bioink reservoirs with organ-specific cells, blood vessel cells, and support medium and load them into the printer; 6) bioprint; and 7) place the bioprinted organ in a bioreactor prior to transplantation.¹³ Laser printers have also been employed in the cell printing process, in which laser energy is used to excite the cells in a particular pattern, providing spatial control of the cellular environment.¹³

Although tissue and organ bioprinting is still in its infancy, many studies have provided proof of concept. Researchers have used 3D printers to create a knee meniscus, heart valve, spinal disk, other types of cartilage and bone, and an artificial ear.^{4.6.7} Cui and colleagues applied inkjet 3D printing technology to repair human articular cartilage.¹³ Wang et al used 3D bioprinting

technology to deposit different cells within various biocompatible hydrogels to produce an artificial liver.¹³ Doctors at the University of Michigan published a case study in the *New England Journal of Medicine* reporting that use of a 3D printer and CT images of a patient's airway enabled them to fabricate a precisely modeled, bioresorbable tracheal splint that was surgically implanted in a baby with tracheobronchomalacia.² The baby recovered, and full resorption of the splint is expected to occur within three years.²

Challenges in Building 3D Vascularized Organs

Proof-of-concept studies regarding bioprinting have been performed successfully, but the organs that have been produced are miniature and relatively simple.^{1,9,10} They are also often avascular, aneural, alymphatic, thin, or hollow, and are nourished by the diffusion from host vasculature.^{1,6,9,10} However, when the thickness of the engineered tissue exceeds 150–200 micro meters, it surpasses the limitation for oxygen diffusion between host and transplanted tissue.¹⁰ As a result, bioprinting complex 3D organs will require building precise multicellular structures with vascular network integration, which has not yet been done.⁶

Most organs needed for transplantation are thick and complex, such as the kidney, liver, and heart.¹¹ Cells in these large organ structures cannot maintain their metabolic functions without vascularization, which is normally provided by blood vessels.¹³ Therefore, functional vasculature must be bioprinted into fabricated organs to supply the cells with oxygen/gas exchange, nutrients, growth factors, and waste-product removal—all of which are needed for maturation during perfusion.^{10,13} Although the conventional tissue engineering approach is not now capable of creating complex vascularized organs, bioprinting shows promise in resolving this critical limitation.¹⁰ The precise placement of multiple cell types is required to fabricate thick and complex organs, and for the simultaneous construction of the integrated vascular or microvascular system that is critical for these organs to function.¹⁰

Customized Implants and Prostheses

Implants and prostheses can be made in nearly any imaginable geometry through the translation of x-ray, MRI, or CT scans into digital .stl 3D print files.^{2,3,6} In this way, 3D printing has been used successfully in the health care sector to make both standard and complex customized prosthetic limbs and surgical implants, sometimes within 24 hours.^{3,7,9} This approach has been used to fabricate dental, spinal, and hip implants.³Previously, before implants could be used clinically, they had to be validated, which is very time-consuming.³

The ability to quickly produce custom implants and prostheses solves a clear and persistent problem in orthopedics, where standard implants are often not sufficient for some patients,

particularly in complex cases.³ Previously, surgeons had to perform bone graft surgeries or use scalpels and drills to modify implants by shaving pieces of metal and plastic to a desired shape, size, and fit.^{3.7} This is also true in neurosurgery: Skulls have irregular shapes, so it is hard to standardize a cranial implant.³ In victims of head injury, where bone is removed to give the brain room to swell, the cranial plate that is later fitted must be perfect.⁹Although some plates are milled, more and more are created using 3D printers, which makes it much easier to customize the fit and design.³

BARRIERS AND CONTROVERSIES

Unrealistic Expectations and Hype

Despite the many potential advantages that 3D printing may provide, expectations of the technology are often exaggerated by the media, governments, and even researchers.³ This promotes unrealistic projections, especially regarding how soon some of the more exciting possibilities—such as organ printing—will become a reality.³ Although progress is being made toward these and other goals, they are not expected to happen soon.^{3,4} 3D printing will require vision, money, and time for the technology to evolve into the anticipated applications.³ While it is certain that the biomedical sector will be one of the most fertile fields for 3D printing innovations, it is important to appreciate what has already been achieved without expecting that rapid advances toward the most sophisticated applications will occur overnight.³

Safety and Security

3D printing has given rise to safety and security issues that merit serious concern.^{8,11} 3D printers have already been employed for criminal purposes, such as printing illegal items like guns and gun magazines, master keys, and ATM skimmers.^{7,11} These occurrences have highlighted the lack of regulation of 3D printing technology.⁷ In theory, 3D printing could also be used to counterfeit substandard medical devices or medications.¹² Although 3D printing should not be banned, its safety over the long term will clearly need to be monitored.⁷

In 2012, in response to the news that a functioning plastic handgun had been 3D printed, several local and state legislators introduced bills banning access to this technology.⁸ However, such fear-based policy responses could stifle the culture of openness necessary for 3D printing to thrive.⁸ Such a ban could push 3D printing underground at the expense of important scientific, medical, and other advances.⁸ There have already been reports of "garage biology" being conducted that could potentially lead to innovations in the life sciences.⁸ However, it is being conducted in secrecy to avoid interference from law enforcement—even though the research is legal.⁸

Reading Comprehension Questions

- 1. What is "bioprinting" and how does it work?
- 2. Summarize the different ways how beneficial 3D printing can be in the medical field. Give a concrete example of each.

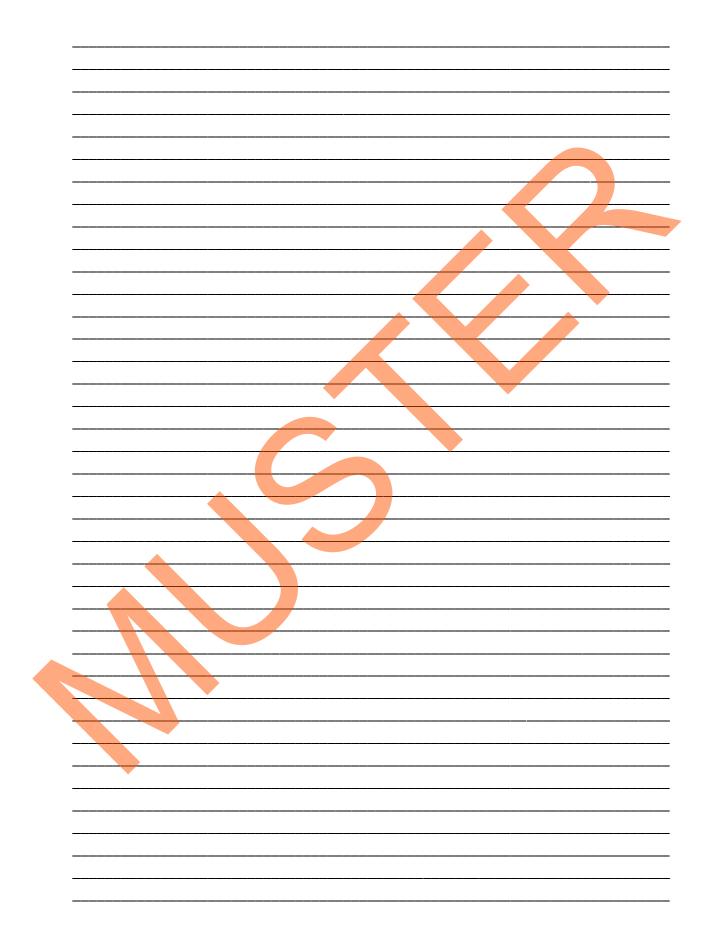
- 3. What is the biggest problem thus far with bioprinting living organs? Why is it a problem?
- 4. Discuss why there is such a hype around 3D printing and bioprinting. Include evidence from throughout the article.

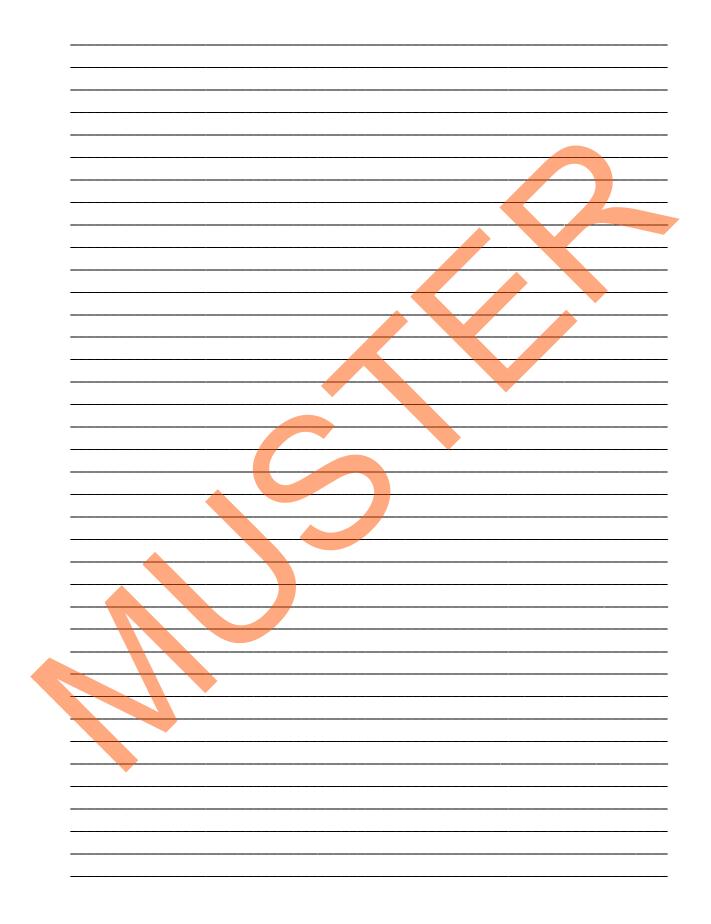


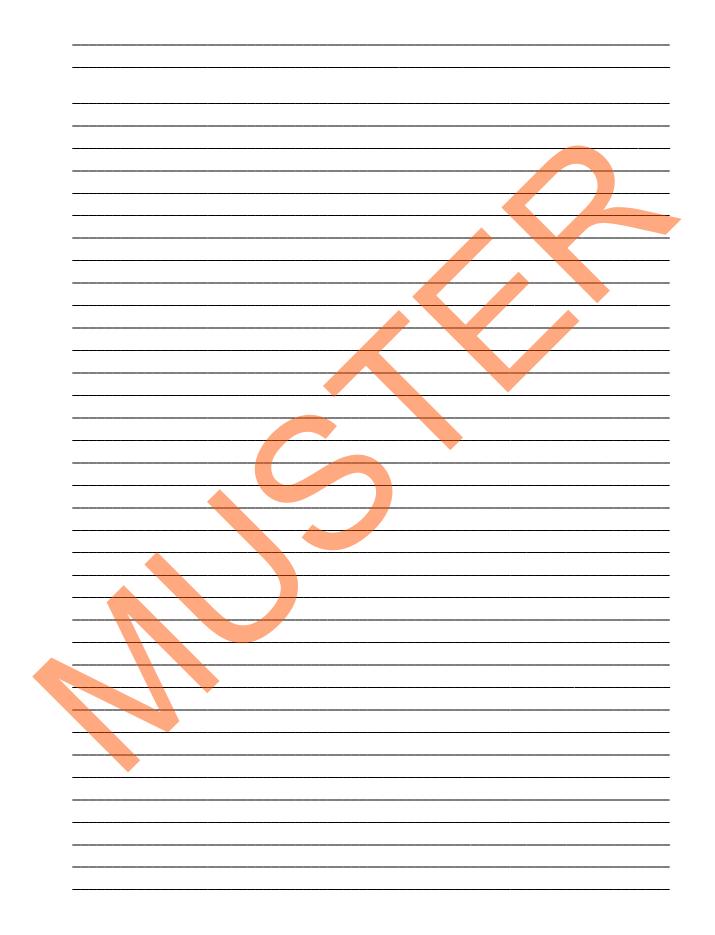
Part 4: Case Study Writing

You are a journalist for a scientific magazine, and you've been asked to write a report defending whether or not you agree with the politician and his agenda. Support your opinion using information you've gathered. Then, include a section in which you advocate one biotechnological advancement over the other (cloning vs 3D bioprinting) and why, and discuss whether there are moral/ethical differences or similarities. Your report structure must include the following: Introduction, Findings, Opinion & Reasons, Preferred technology, and a Conclusion. Please write your report in the space provided. You will have 90 minutes to plan, write, and revise your report. This section of the test covers 25% of the overall exam grade.

Title:	









Part 5: Case Study Speaking

In answer to one of the topics below, prepare a well-structured PowerPoint presentation for the length of 25-30 minutes. In addition to using the case study materials from earlier in this exam, you should also include your own online sources for more information. Cite your sources. This section of the test covers 25% of the overall exam grade.

Topic 1:

Present the effects 3D printing, both normal and bioprinting, may have on medicine and/or nutrition. Include positive as well as negative effects. Make your own predictions, and explain how you came to those conclusions with current evidence.

Topic 2:

Present your argument for or against the enthusiastic, embryonic stem cell research politician. Give facts and evidence for your stand point.

Topic 3:

There are many medical difficulties which consistently arise with cloning. Present what these problems are in detail. Then, discuss whether or not you feel this field should continue its research, i.e. is it all really worth it?

Topic 4:

A small, extremely religious family just survived a terrible car accident, but not without their 12 year old daughter receiving injuries to the head, serious damage to her face and losing her left ear. Doctors say they can repair some of the damage as well as replace her ear using a 3D bioprinter, for which they need her stem cells. The family feels uneasy about the procedure for religious reasons, but is willing to listen before saying no. Prepare an argumentative/persuasive presentation. Introduce 3D bioprinting to the family, how it works and what it entails, and its benefits and risks in the field of medicine, as well as for their daughter.