LECTURE 1: INTRODUCTION

1. Introduction

Artificial organs can be defined as products that are intended to be used for the (partly) support, replacement or regeneration of diseased, damaged or otherwise not fully functional organs.

- For patients with severely damaged organs, who are on a waiting list for a transplant organ, the availability of artificial organs could be the only way to survive.
- One way of creating artificial organs is the use of cell therapy and/or tissue-engineering techniques.
- Also, medical device solutions based on mechanical, optical, electrical, physical or other technological characteristics can be applied, as well as combination products using distinct features from both devices and cell products.

1.1 PURPOSE

- providing life support to prevent imminent death while awaiting a transplant (e.g. artificial heart);
- dramatically improving the patient's ability for self-care (e.g. artificial limb);
- improving the patient's ability to interact socially (e.g. cochlear implant); or
- Improving a patient's quality of life through cosmetic restoration after cancer surgery or an accident.

The use of any artificial organ by humans is almost always preceded by extensive experiments with animals. Initial testing in humans is frequently limited to those either already facing death or who have exhausted every other treatment possibility.

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1.2 Design considerations and evaluation process:

- establish the specification for the device i.e. the function and the physical constraints.
- Defining specifications and constraints is the first step in the conceptualization of an artificial organ.
- think realistically about design alternatives, the limitations of available materials, and the clinical constraints which will apply.
- the construction of a prototype.
- usually, it exhibits some level of performance and durability which falls, either because of some misjudgment in terms of required function or because of some unanticipated problem arising at the interface between the device and the body.
- The following step of development called optimization, where new experiments are needed to establish the reliability and effectiveness of the device in animal models.
- This is the stage of validation of the device, which is first conducted in acute experiments and must later be extended to periods of observation approximating the duration of intended use in humans.
- The final stage, is individualization, that is, the ability to fit the needs of diverse individuals. Human come in a wide range of body sizes.

1.3 Evaluation process:

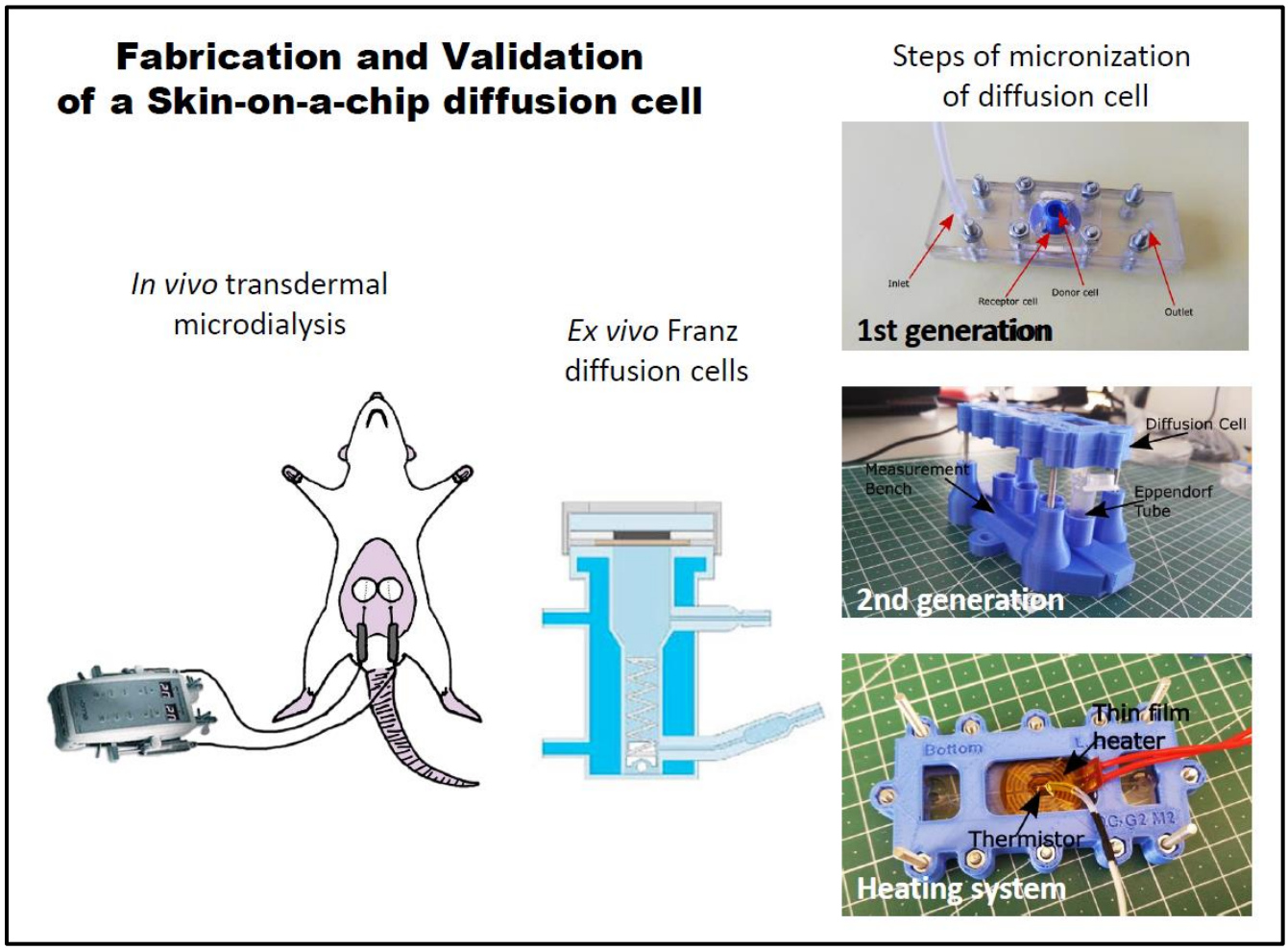
The evaluation process of an artificial organ typically is done in six phases:

1.3.1 In vivo bench testing:

In vivo bench testing of a completed prototype has three major purposes:

1. To observe the mode of operation of the device and assess its performance under tightly controlled circumstances

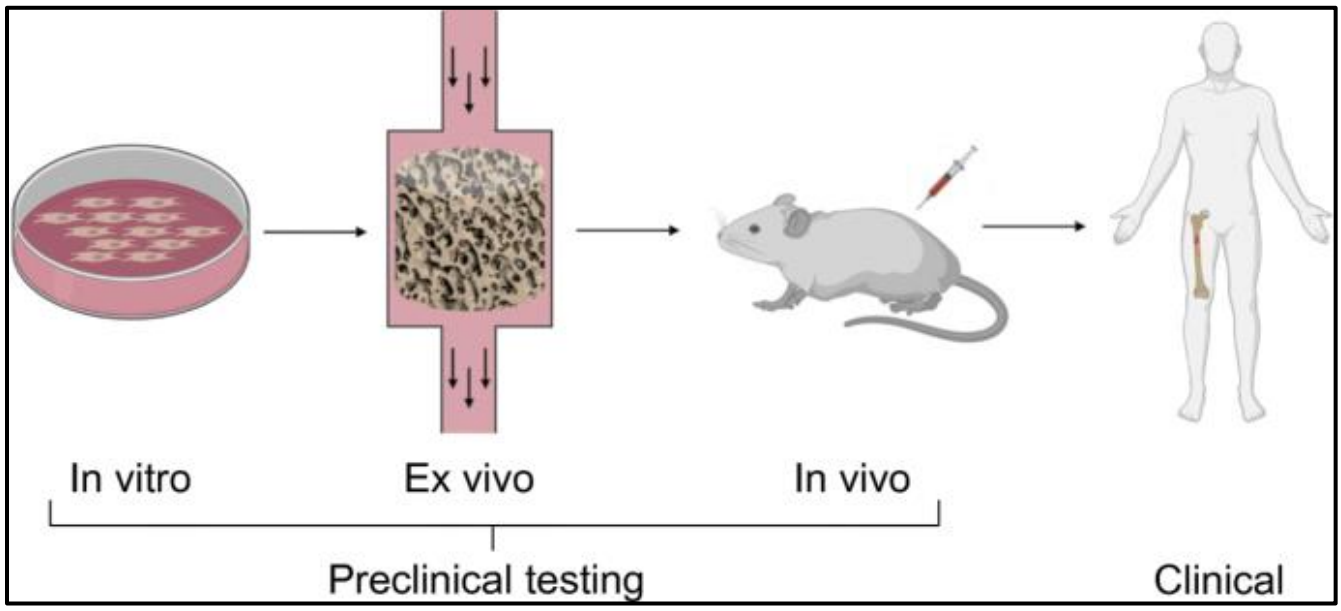
2. To define performance in quantitative terms over a wide range of environmental or input conditions
3. To assess the device's reliability and durability in a manner which can be extrapolated to the intended clinical use



1.3.2 Ex vivo appraisal:

Because of the difficulty of keeping blood in its physiologic state in a container, the evaluation of some blood processing or blood contacting devices in performed by connecting them through the skin to an artery or vein or both if the blood must be returned to the cardiovascular system to avoid excessive hemorrhage.

Such experiments retain the advantage of keeping the device under direct observation while allowing longer experiments than are feasible in vitro, particularly if the animal does not require general anesthesia.

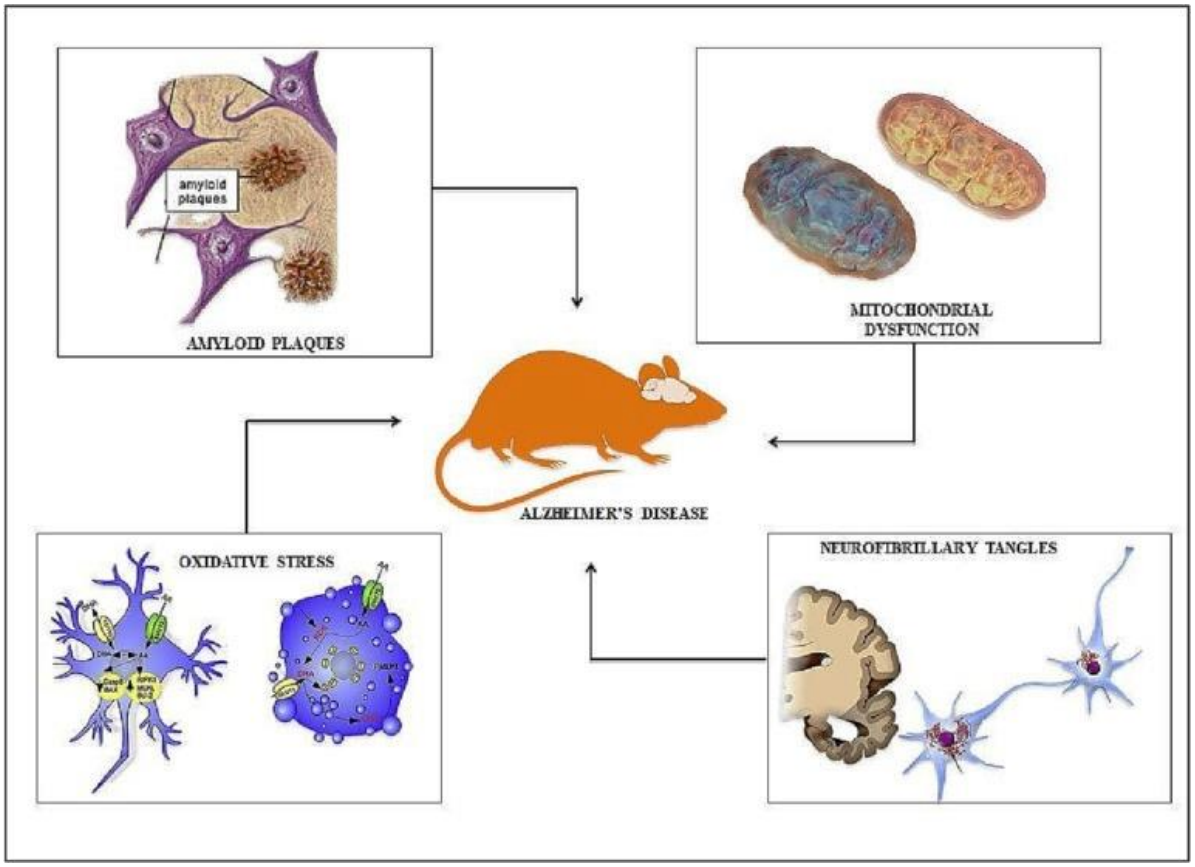


1.3.3 In vivo evaluation with health experimental animals:

- There comes a stage in the development of most devices where they must be assessed to their target location in a living body.
- The matching of device size and shape with available experimental sites in the location in a living body.
- The matching of device size and shape with available experimental sites in the appropriate animal species is a necessary condition.
- Such experiments typically last weeks, months, or years and provide information about body- device and tissue-material interactions.
- Rodents, felines, and dogs raised for research purposes are usually too small for the evaluation of human sized devices.
- Farm animals such as sheep, goats, pigs and claves are commonly used.

1.3.4 In vivo evaluation with animal models of disease:

- A first approximation of the effectiveness of a device in replacing a physiologic function can obtained after removing the target organ in a normal animal.
- However, when the organ failure is only the cardinal sign of a complex systemic disease, the interactions between device and the persisting manifestations of the disease occur spontaneously in some species and in other cases can be obtained by chemical, physical or surgical intervention, where such models of disease exist in animals which can be fitted with a device, useful information is obtained which helps to refine the final prototype.



Animal models of Alzheimer's disease

1.3.5 Controlling clinical trials:

- Once reliability and effectiveness have been established through animal experiments and the device appears to meet a recognized clinical need, a series of clinical trials is undertaken.
- The first step often concentrates on the demonstration of safety of the device with a careful watch for side effects or complications.
- Then, a controlled clinical trial will be carried out with patients to evaluate effectiveness as well as safety on a scale which allows statistical comparison with a control form of treatment.
- This protocol may extend from a few months to several years depending upon the expected benefits of the device and the natural history of the disease.

1.3.6 General clinical use:

Once a device is deemed successful by a panel of experts, it may be approved by regulatory agencies for commercial distribution.

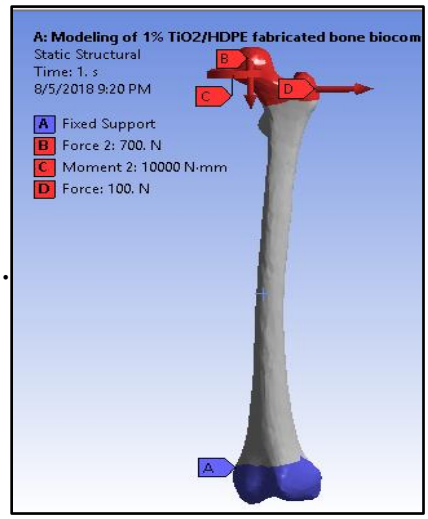
Increasingly a third stage of clinical evaluation appears necessary, namely post market surveillance, that is a system of clinical outcomes analysis under conditions of general availability of the device to a wide range of doctors and patients.

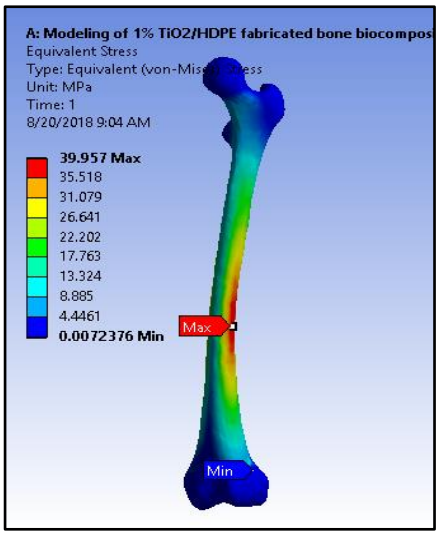
1.4 Artificial ORGANS EXAMPLES

The following paragraphs contain the developments for each organ in summary:

1.4.1 Artificial limbs - Artificial arms and legs, or prosthetics, are intended to restore a degree of normal function to amputees.

- Mechanical devices that allow amputees to walk again or continue to use two hands have probably been in use since ancient times.
    - New plastics and other materials, such as carbon fiber have allowed artificial limbs to become stronger and lighter, limiting the amount of extra energy necessary to operate the limb.
    - Additional materials have allowed artificial limbs to look much more realistic.
    - New advances in artificial limbs include additional levels of integration with the human body.
    - Electrodes can be placed into nervous tissue, and the body can be trained to control the prosthesis.





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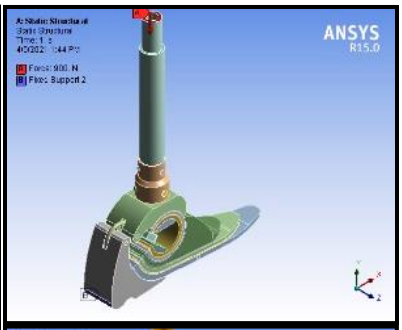

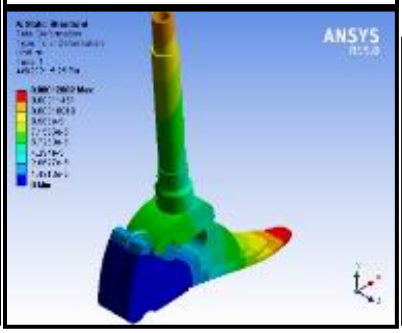

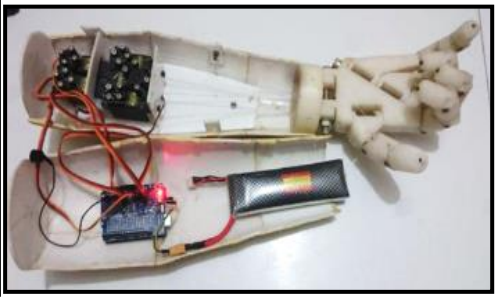

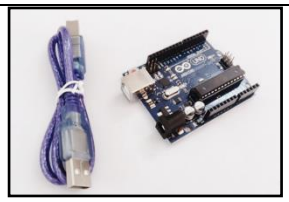	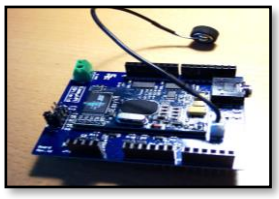
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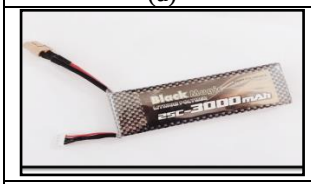	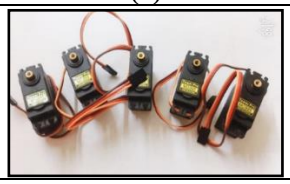
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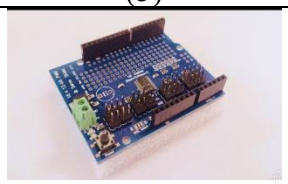	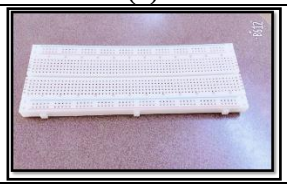
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	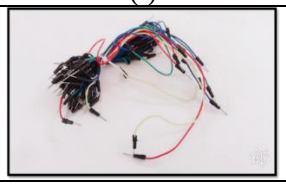
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