Synthetic Human Tissue Models Can Reduce the Cost of Device Development

Synthetic human tissues and body parts that closely resemble the live human environment have been developed for use in medical device verification and validation studies. This article discusses how they can save developers time and money while improving quality and accuracy.

Dr. Christopher Sakezles
SynDaver Labs, Tampa, Florida, USA

Need for faster innovation

The United States (US) medical device manufacturing market generates in excess of $85 billion USD (approximately €66.5 billion) in annual sales.[1] In addition, the US medical device industry is emerging as the most reliable worldwide growth area in medical technology. With the median age of the population increasing steadily, the industry is expected to be resilient during the current downturn.[2]

In addition, while the industry is growing, it is also restructuring. Five major interrelated trends that will shape the future of the industry are: continued and increasing cost pressures, a need for efficiency in innovation, increased outsourcing and offshoring, networked automation and growth in consumer-directed health care. It is estimated that the US industry spends more than $5 billion USD (approximately €3.8 billion) per annum on testing new medical devices and a substantial additional amount on research and development (R&D). Cost pressures will continue to intensify as companies explore new ways to reduce costs, streamline operations and acquire new technology to innovate current operations. The medical device industry needs new technology that will improve the testing of new medical devices as well as allow for a substantial

reduction in R&D expenditure, and eliminate wasted time, money and effort trying to bring a new product to market. A new technology by SynDaver Labs (www.syndaver.com) that will trim time, expenditure and manpower while improving the quality and accuracy of testing medical devices has been developed. It provides synthetic human tissues and body parts to replace traditional bench top fixtures, human cadavers and even live animals in medical device design verification and validation studies.

Current methods

Current design verification and validation testing platforms include bench top fixtures (rubber tubing, plastic and glass components, etc), human cadavers, and live animals. None of these perfectly replicate the end-use environment for the device, which is generally a living human

body. In addition, although a test using such models can be cost efficient for a company, the results and data may be of little actual use. Engineers predict the performance of a device in vivo by interpreting data drawn from in vitro results, and as the differences between the actual use environment (the patient) and the model (the in vitro test) grow larger, the reliability of the resulting data as a predictor of actual performance is reduced.

Testing on a live animal that has some physiological similarities to the human environment has advantages. However there are various ways in which it does not replicate actual end use conditions, and there are several well-defined drawbacks. Using live animals makes it almost impossible to obtain consistent, reproducible results because of variations from animal to animal and test to test. Testing on live animals carries a financial and ethical burden that can make testing unfeasible for smaller medical device companies and testing organisations. For a company to test on live animals, it must comply with the relevant national Animal Welfare Act and other international protocols. These requirements add a huge overhead that makes each data point cost several times the expense of the animal alone. In the US, single data point animal studies often cost well over $10,000 USD.

Human cadavers offer an anatomically accurate testing medium, although death and chemical preservation significantly change the physical characteristics of the tissue and make it respond inaccurately to stimulus. In addition cadavers are rare, expensive and become damaged during repeated testing.

Synthetic human parts

The synthetic human tissues and body parts developed by Syndaver Labs meet the need for a more reliable, consistent, realistic and cost-effective solution. The technology incorporates replaceable muscles, tendons, veins, arteries and organs, which are manufactured from a library of materials that replicate the anatomical structure and physical properties of living tissue. The exact formula varies for each material (skeletal muscle differs from cardiac muscle, skin differs from fascia latae, etc), but in general it includes water, microfibres, macrofibres, fibre meshes, binders and a variety of salts. They are designed primarily for use in medical device verification and validation tests. The end-products made from these synthetic tissues closely resemble the actual live human environment and may be utilised as direct replacements for traditional models in simulated use testing. Examples of how these products have been employed include ear models used in developing a device designed to traverse the

tympanic membrane, eye models used to develop glaucoma implants, tissue plates used in the development of femoral puncture closure and laproscopic devices, arm and leg models used in the development of wound control treatments, and vascular models used to develop needles, guidewires and catheters.

Individual models are constructed so that they mimic both the geometry (density, shape, length and diameter) and physical properties (water, salt and fibre content, modulus in tension, compression, and shear, coefficient of static or dynamic friction, surface energy, dielectric properties) of the portion of the human anatomy they are designed to match.

While the technology is designed to simulate a specific portion of the human anatomy, individual synthetic tissue formulations are not based on tests performed on human tissues. Instead, live animal models (generally porcine) are employed as the primary design basis for

all of the synthetic tissues. In addition, each component of a given model is fabricated so that the interaction between adjacent components is similar to that of the target anatomy. Finally, individual anatomical components such as muscles, veins and arteries are removable and replaceable. Any replacement synthetic component will react identically to the component that it has replaced; this saves time and costs, because tests would not have to be rerun if a component needs to be replaced during a batch of data gathering.

Construction of the models

SynDaver Labs' synthetic human body parts are developed in discrete sections, and multiple components are generally required to fabricate a specific model such as a thoracic aorta. For this example, the aorta is conceptually divided into two separate components: the aorta itself and the surrounding tissues. Using this concept, the simplest aorta model would require at least two different tissue analogues (a synthetic tissue that mimics actual tissue) to model the performance of the target anatomy.

In reality, more complex models require a larger number of analogues to accurately replicate the response of a target tissue. The physical response to any kind of action such as penetration by a needle, abrasion by a catheter or expansion by a balloon cannot be adequately modelled by a simple rubber tube. Human arteries incorporate multiple layers, thus they respond differently than they would if they were made from a single monolithic material. SynDaver Labs' synthetic human arteries simulate this complex response by using discrete tissue analogues for the intima, media and adventitia layers. These materials are then assembled into a composite construction that accurately mimics a real artery.

Live tissue testing

To design a specific tissue analogue, first the modelled properties and data source are defined. The modelled properties are set by selecting and prioritising the chemical, physical and mechanical properties that the analogue is required to mimic, and the set of properties is dependent on the type of device under test, the target anatomy and the test objectives.
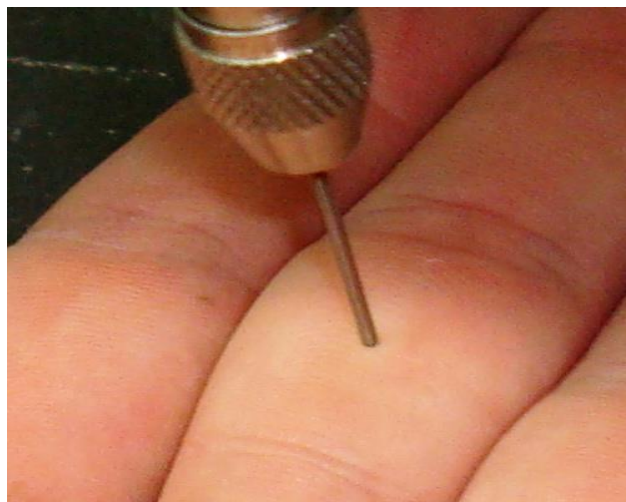
In the case of testing the damage to the arterial intima that is caused by a device traversing the femoral artery, abrasion resistance would be a primary consideration in the list of tests for the tissue analogue. An additional target property could be included to simulate the tendency of the device to penetrate the arterial wall by running a penetration resistance or shear strength property test. A particular component can have any number of properties to be tested, although it is advisable to limit the number of design requirements to specific items related to a particular series of tests to be performed.

A decision must also be made during the design process as to whether an analogue is to mimic human or animal tissue. A data source for the tissue properties must then be defined by either utlising data from literature or by generating it directly (by performing the appropriate tests on tissue samples). Unfortunately, data drawn from literature is collected under a wide variety of conditions, and almost always involve tests performed on cadaver tissue. SynDaver Labs generates test data directly from live animal tissue, then uses the designed synthetic tissues to build human anatomy.

Each live tissue test is performed under strictly controlled conditions to ensure test validity and to allow candidate tissue analogue tests to be replicated under identical conditions. Because results of tests are critical to the replication and design of analogues, it is a strict requirement that tissue sample tests are performed, as opposed to using data from literature. This allows for the tight control of the tissue harvest, sample preparation, test design and the testing methods that are utilised. Once the required targeted properties have been finalised and the source of data (literature or relative tissue sample testing) has been selected, the series of tests can begin.

The test data are then utilised for the final design and construction of the analogue. The various items listed as targeted properties are prioritised so that the model can incorporate the highest priority properties. The more properties that are incorporated in a model, the more complex the structure will need be to meet all the priorities. If a model requires more than two or three properties, separate analogues must generally be designed to model these. A component that is comprised of several analogues will exhibit a more complex and realistic response than a component constructed from a single analogue.

For example, a synthetic rectus femoris muscle would ideally consist of three separate analogues with two target properties as opposed to one single analogue with six properties. A synthetic artery model would be composed of three separate interconnected tissue analogues (for intima, media and adventitia). The components are constructed of proprietary materials that exactly replicate the properties of the anatomical structure they are intended to replace. The construct materials are formulated to replicate specific tissues (muscle, tendon, intima) so that the fabricated anatomical structures will contain the appropriate levels of fibre, water and salts and will exhibit a given combination of physical properties such as electrical conductivity, abrasion resistance, modulus, strength and coefficient of friction. The materials utilised in fabrication are suitable for modeling vascular intima, epithelia and many other soft tissues.

Before any one of these synthetic tissues are released for use, it is validated at both the tissue and component level. Tissue level validation compares the physical and mechanical properties of the synthetic tissue analogue to the living tissue sample on which the analogue was based. Both sets of data are collected under identical conditions so that validity is assured. Component level validation compares the structure and overall performance of a complex synthetic composite (such as an organ, muscle or artery) to the target anatomy on which the analogue was based. It would include items such as measuring force required to puncture the wall or testing the pressure required to dilate the artery to a predetermined size. All components must agree with the living tissue samples within 10% to be considered valid.

A winning technology

The synthetic human tissues and body parts developed by SynDaver Labs facilitate the generation of performance data with less time and money spent on the development programme. This technology eliminates biohazard exposure, there are no special training requirements involved and no need to hire outside specialists. Using this technology to replace current models in medical device verification and validation can result in simplified tests and

raise validation scores. By employing the technology early in the development process, vital feedback on performance may be collected before erroneous assumptions adversely affect the device's design and thereby the probability of costly late stage design changes is reduced. The models may be used in standard laboratory settings.

These synthetic parts address many of the requirements to reduce device testing and validation and verification costs and the person hours involved in bringing a new device from concept to production. The technology is used in the US by Fortune 500 medical device companies and SynDaver Labs has received an "Excellence in Innovation" award from the US Department of Commerce.[3] The company has secured three US patents for this technology and has additional US and European patent applications pending.

References

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7886 Woodland Center Blvd
Tampa, Florida 33614
Phone: 813-600-5530
Fax: 813-600-3235
Email: info@syndaver.com
Web: www.syndaver.com