Module - 3

HUMAN ORGAN SYSTEMS AND BIO-DESIGNS - 2 (QUALITATIVE):

Lungs as purification system (architecture, gas exchange mechanisms, spirometry, abnormal lung physiology - COPD, Ventilators, Heart-lung machine). Kidney as a filtration system (architecture, mechanism of filtration, CKD, dialysis systems). Muscular and Skeletal Systems as scaffolds (architecture, mechanisms, bioengineering solutions for muscular dystrophy and osteoporosis).

HUMAN ORGAN SYSTEMS AND BIO ORGANS – I:

LUNGS AS A PURIFICATION SYSTEM:

Introduction:
Every cell in your body needs oxygen to live. The air we breathe contains oxygen and other gases. The respiratory system's main job is to move fresh air into your body while removing waste gases. Once in the lungs, oxygen is moved into the bloodstream and carried through your body. At each cell in your body, oxygen is exchanged for a waste gas called carbon dioxide. Your bloodstream then carries this waste gas back to the lungs where it is removed from the bloodstream and then exhaled. Your lungs and the respiratory system automatically perform this vital process, called gas exchange.
In addition to gas exchange, your respiratory system performs other roles important to breathing. These include:

- Bringing air to the proper body temperature and moisturizing it to the right humidity level.
- Protecting your body from harmful substances. This is done by coughing, sneezing, filtering, or swallowing them.
- Supporting your sense of smell.

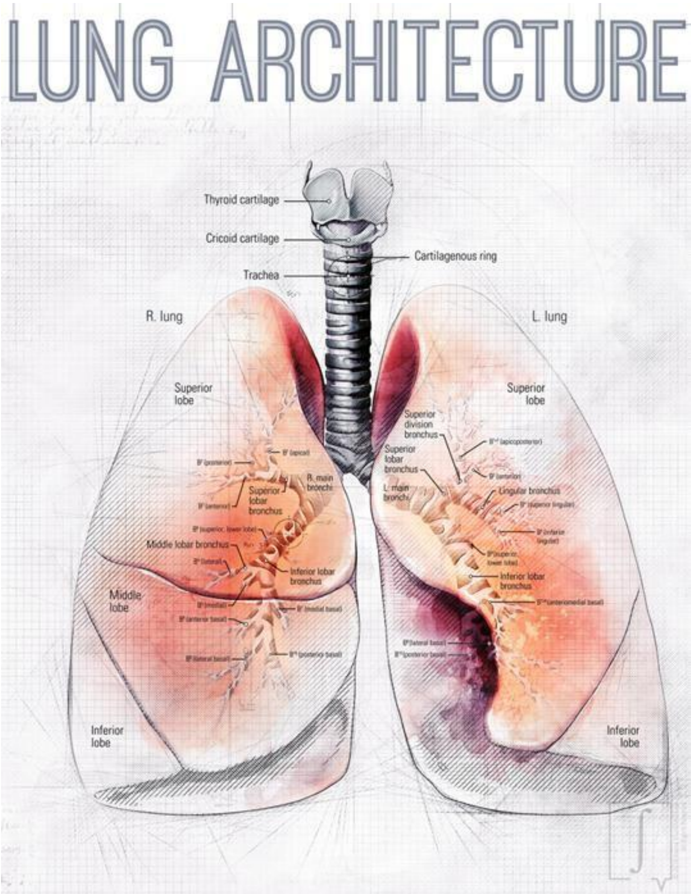
Lungs help in the purification of blood. Arteries carry pure oxygenated blood from the heart to other parts of the body. Veins carry impure venous blood back from other parts of the body to the right side of the heart. This impure blood goes to the lungs for purification.
When the breath is inhaled, oxygen from the air comes in contact with the impure blood and the blood takes up oxygen. The waste matter in the blood releases carbonic acid and the blood is purified. The purified blood is carried to the heart by the veins.

Architecture:
The lung parenchyma is mainly comprised of numerous air-containing passages and intervening fine structures, corresponding to alveolar ductal lumens and alveoli, as well as alveolar septa and small pulmonary vessels occupying 10% of total parenchymal volume.
The primary function of the lungs is gas exchange. However, the lungs perform several important

non-respiratory functions that are vital for normal physiology.

The lung, with its unique ability to distend and recruit pulmonary vasculature, acts as a reservoir of blood, fine-tuning preload to the left heart to optimize cardiac output.

- The lung acts as a filter against endogenous and exogenous emboli, preventing them from accessing systemic circulation.
- Pulmonary epithelium forms the first line of defense against inhaled particles.
- Pulmonary endothelial cells are responsible for the uptake, metabolism, and biotransformation of several exogenous and endogenous substances.
- Pulmonary metabolic capacity is easily saturated, but pulmonary endothelial binding of some drugs alters their pharmacokinetics.



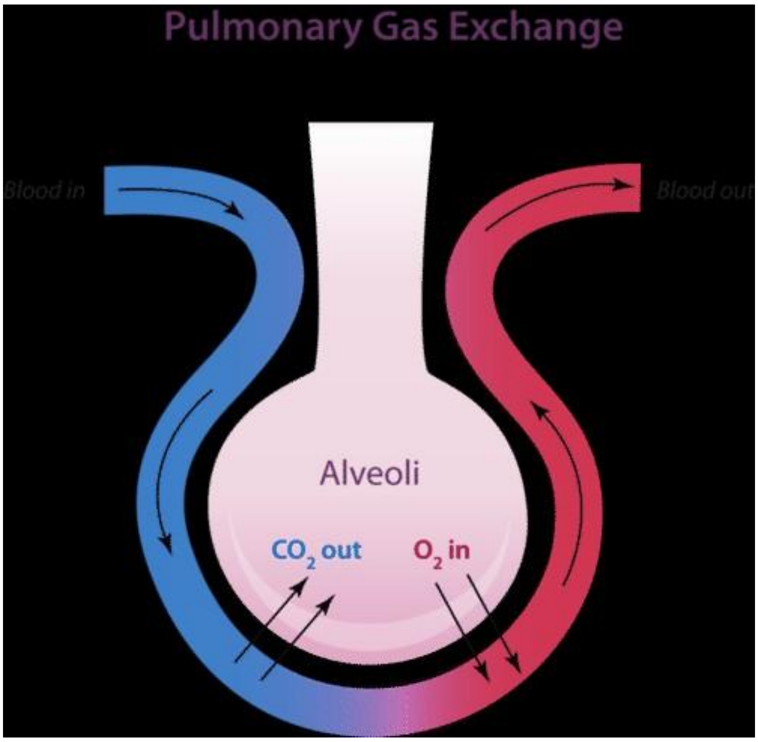
COURTESY: *EDWARD RUDOLF WEIBEL*

GAS EXCHANGE MECHANISMS:

Air enters the body through the mouth or nose and quickly moves to the pharynx or throat. From there, it passes through the larynx, or voice box, and enters the trachea.

The trachea is a strong tube that contains rings of cartilage that prevent it from collapsing. Within the lungs, the trachea branches into a left and right bronchus. These further divide into smaller and smaller branches called bronchioles. The smallest bronchioles end in tiny air sacs. These are called alveoli.

They inflate when a person inhales and deflate when a person exhales. During gas exchange oxygen moves from the lungs to the bloodstream. At the same time, carbon dioxide passes from the blood to the lungs. This happens in the lungs between the alveoli and a network of tiny blood vessels called capillaries, which are located in the walls of the alveoli.



ILLUSTRATED BY *D.M. GOMEZ*

The walls of the alveoli share a membrane with the capillaries. That's how close they are. This lets oxygen and carbon dioxide diffuse, or move freely, between the respiratory system and the bloodstream.

Oxygen molecules attach to red blood cells, which travel back to the heart. At the same time, the carbon dioxide molecules in the alveoli are blown out of the body the next time a person exhales. The gas exchange allows the body to replenish the oxygen and eliminate carbon dioxide. Doing both is necessary for survival.

SPIROMETRY:

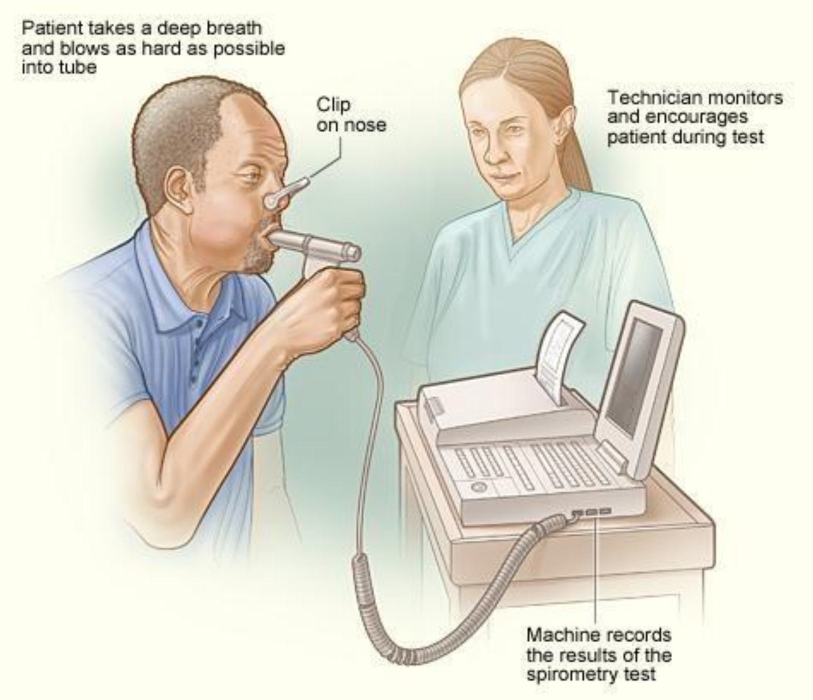
Spirometry (spy-ROM-uh-tree) is a common office test used to assess how well your lungs work by measuring how much air you inhale, how much you exhale, and how quickly you exhale. Spirometry is used to diagnose asthma, chronic obstructive pulmonary disease (COPD), and other conditions that affect breathing.

175 years have elapsed since John Hutchinson introduced the world to his version of an apparatus that had been in development for nearly two centuries, the spirometer.

Spirometers can be divided into two basic groups:

• Volume-measurement devices (e.g. wet and dry spirometers).

• Flow-measurement devices (e.g. pneumotachograph systems, mass flow meters).

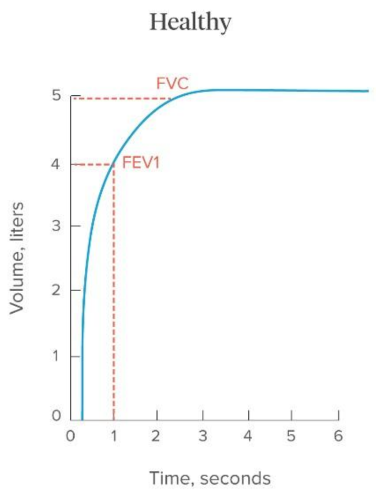


Requirements of an acceptable spirometer are:

• Spirometers must be able to accumulate volume for ≥15 s.
• The measuring volume should be ≥8 L (body temperature and pressure, saturated).
• The accuracy of reading should be at least ±3% (or ±0.05 L) with flows from 0–14 L per s.
• The total resistance to airflow at 14 L per s should be <1.5 cmH2O per L per s (<0.15 kPa per L per s).

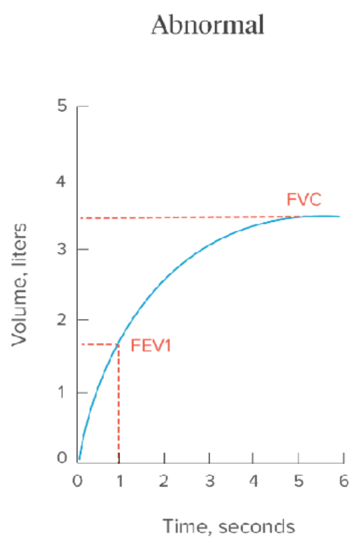
HOW TO CALCULATE THE NORMAL RATE OF RESPIRATION IN A SPIROMETER:

The FEV1/FVC Ratio (FEV1%) parameter is calculated by dividing the measured FEV1 value by the measured FVC value. The Measured column shows the absolute (numerical) ratio, and the Predicted column shows the ratio expressed as a percentage. In healthy adults of the same gender, height, and age, the normal Predicted percentage should be between 70% and 85%.



ABNORMAL LUNG PHYSIOLOGY:

Percentages lower than 70% are considered abnormal. This is an important measurement because obstructive diseases such as COPD, chronic bronchitis, and emphysema cause increased airway resistance to expiratory airflow, and may result in percentages of 45% to 60%. Restrictive diseases such as pulmonary fibrosis tend to reduce both FEV1 and FVC values, so the percentage can remain within the normal range, or even increase.



COPD:

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. Symptoms include breathing difficulty, cough, mucus (sputum) production, and wheezing. It's typically caused by long-term exposure to irritating gases or particulate matter, most often from cigarette smoke. People with COPD are at increased risk of developing heart disease, lung cancer, and a variety of other conditions.
Emphysema and chronic bronchitis are the two most common conditions that contribute to COPD. These two conditions usually occur together and can vary in severity among individuals with COPD.

Symptoms:
COPD symptoms often don't appear until significant lung damage has occurred, and they usually worsen over time, particularly if smoking exposure continues.

Signs and symptoms of COPD may include:
- Shortness of breath, especially during physical activities
- Wheezing
- Chest tightness
- A chronic cough that may produce mucus (sputum) that may be clear, white, yellow, or greenish
- Frequent respiratory infections
- Lack of energy
- Unintended weight loss (in later stages)
- Swelling in ankles, feet, or legs

Tests may include:
- Lung (pulmonary) function tests.
- Chest X-ray.
- CT scan.
- Arterial blood gas analysis.
- Laboratory tests.

Medications:
Several kinds of medications are used to treat the symptoms and complications of COPD. You may take some medications regularly and others as needed.
- Bronchodilators
- Inhaled steroids
- Combination inhalers
- Oral steroids
- Phosphodiesterase-4 inhibitors
- Theophylline
- Antibiotics

Mechanical ventilation is a lifesaving therapy in patients who have acute respiratory failure due to chronic obstructive pulmonary disease (COPD). Mechanical ventilation either invasive or non-invasive has an important role in the management of acute exacerbation of COPD (AECOPD).

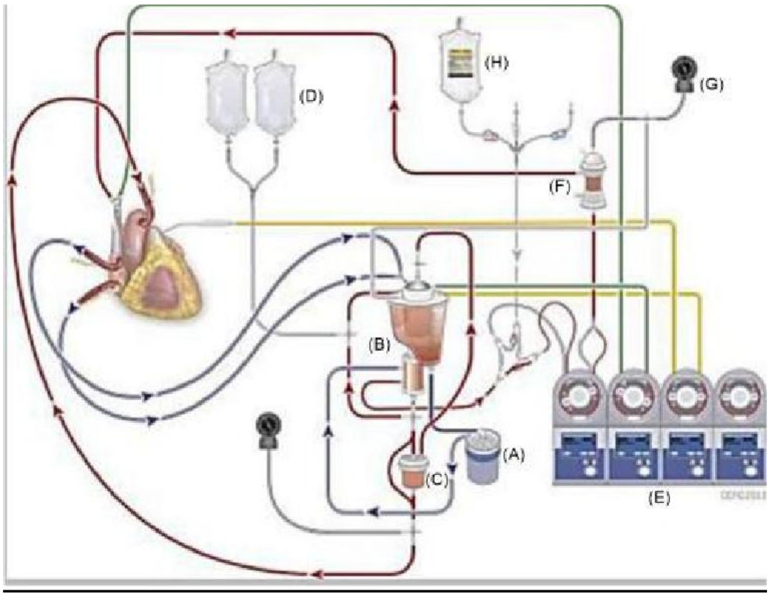
VENTILATOR:

Mechanical ventilators are machines that act as bellows to move air in and out of your lungs. Your respiratory therapist and doctor set the ventilator to control how often it pushes air into your lungs and how much air you get. You may be fitted with a mask to get air from the ventilator into your lungs or you may need a breathing tube if your breathing problem is more serious. When you're ready to be taken off the ventilator, your healthcare team will "wean" you or decrease the ventilator support until you can start breathing on your own.

HEART LUNG MACHINE:

A heart-lung machine is an apparatus that does the work both of the heart (i.e., pumps blood) and the lungs (i.e., oxygenates the blood) during, for example, open-heart surgery The basic function of the machine is to oxygenate the body's venous supply of blood and then to pump it back into the arterial system.

Blood returning to the heart is diverted through the machine before returning to the arterial circulation. Some of the more important components of these machines include pumps, oxygenators, temperature regulators, and filters. The heart-lung machine also provides intracardiac suction, filtration, and temperature control.



Blood drains by gravity or with the use of gentle suction into the oxygenator venous reservoir labeled (B). (A) represents the arterial pump that pumps the blood from the venous reservoir (B) and delivers blood to the membrane oxygenator which is attached to the lower part of the venous reservoir. Once oxygen, carbon dioxide, and heat exchange have occurred the blood is directed thru an arterial blood filter (C). A purge line to the uppermost part of the filter serves for the removal of any microemboli that may have been introduced into the blood during its passage through the circuit. The oxygenated blood is introduced back into the patient's circulatory system through cannulae (a large tube connected to the circuit) placed in the ascending aorta. The line attached to intravenous bags labeled (D) provides a method for priming the CPB circuit with electrolyte fluid or a port for adding blood during bypass. Four roller pumps labeled (E) in the diagram are auxiliary. The one on the far left is used to pump a cardioplegia solution with a mixture of blood and additives, labeled (H), and used to arrest the heart. This solution is cooled with a separate heat exchanger labeled (F).

KIDNEY AS FILTRATION SYSTEM:

Introduction:

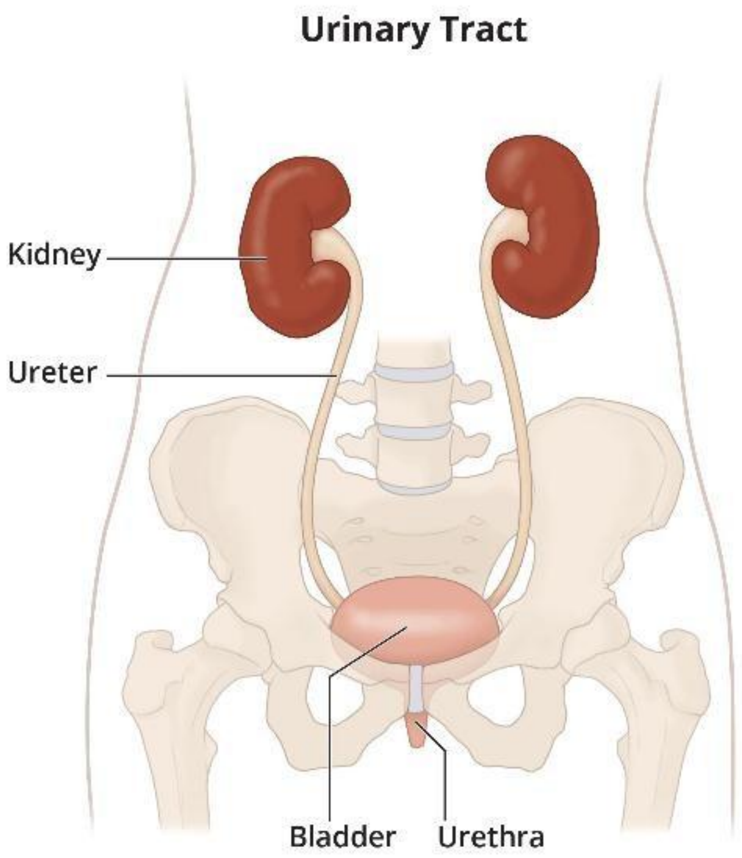
Kidneys remove wastes and extra fluid from the body. Kidneys also remove acid that is produced by the cells of the body and maintain a healthy balance of water, salts, and minerals—such as sodium, calcium, phosphorus, and potassium—in the blood. Without this balance, nerves, muscles, and other tissues in the body may not work normally.

Kidneys also make hormones that help

- Control blood pressure.
- Make red blood cells NIH external link.
- Keeps bones strong and healthy.

Architecture:

The kidneys are two bean-shaped organs, each about the size of a fist. They are located just below the rib cage, one on each side of the spine. Healthy kidneys filter about a half cup of blood every minute, removing wastes and extra water to make urine. The urine flows from the kidneys to the bladder through two thin tubes of muscle called ureters, one on each side of the bladder. Your bladder stores urine. Kidneys, ureters, and bladder are part of your urinary tract.

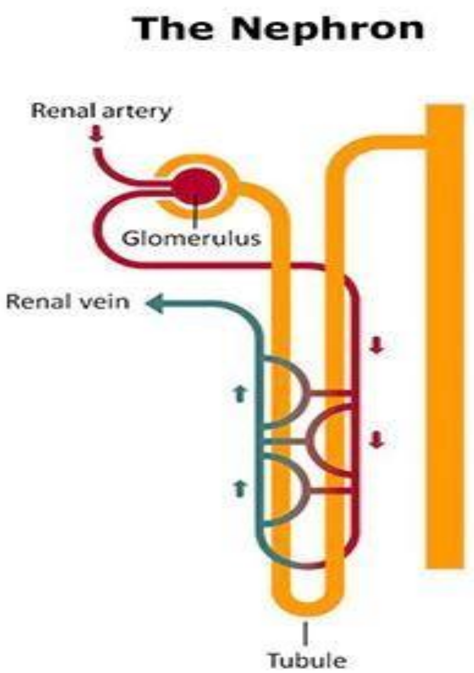


COURTESY: *HANS BACHOFEN*

MECHANISM OF FILTRATION:

Each kidney is made up of about a million filtering units called nephrons. Each nephron includes a filter, called the glomerulus, and a tubule. The nephrons work through a two-step process: the glomerulus filters blood, and the tubule returns needed substances to your blood and removes wastes.

Each nephron has a glomerulus to filter your blood and a tubule that returns needed substances to your blood and pulls out additional wastes. Wastes and extra water become urine.
The glomerulus filters your blood. As blood flows into each nephron, it enters a cluster of tiny blood vessels—the glomerulus. The thin walls of the glomerulus allow smaller molecules, wastes, and fluid—mostly water—to pass into the tubule. Larger molecules, such as proteins and blood cells, stay in the blood vessel. The tubule returns needed substances to your blood and removes wastes.



COURTESY: *SAMUEAL SCHRUCHB*

A blood vessel runs alongside the tubule. As the filtered fluid moves along the tubule, the blood vessel reabsorbs almost all of the water, along with minerals and nutrients your body needs. The tubule helps remove excess acid from the blood. The remaining fluid and wastes in the tubule become urine.

How does blood flow through my kidneys?

Blood flows into the kidney through the renal artery. This large blood vessel branches into smaller and smaller blood vessels until the blood reaches the nephrons. In the nephron, blood is filtered by the tiny blood vessels of the glomeruli and then flows out of the kidney through the renal vein.

Blood circulates through your kidneys many times a day. In a single day, kidneys filter about 150 quarts of blood. Most of the water and other substances that filter through your glomeruli are returned to the blood by the tubules. Only 1 to 2 quarts become urine.

When the kidney doesn't function properly, chronic kidney disease occurs when a disease or condition impairs kidney function, causing kidney damage to worsen over several months or years.

CKD:

Chronic kidney disease includes conditions that damage your kidneys and decrease their ability to keep you healthy by filtering wastes from your blood. If kidney disease worsens, wastes can build to high levels in your blood and make you feel sick. You may develop complications like

- high blood pressure
- anemia (low blood count)
- weak bones

- poor nutritional health
- nerve damage

Symptoms:
People with CKD may not feel ill or notice any symptoms. The only way to find out for sure if you have CKD is through specific blood and urine tests. These tests include the measurement of both the creatinine level in the blood and the protein in the urine.

Treatment:
Depending on the cause, some types of kidney disease can be treated. Often, though, chronic kidney disease has no cure. Treatment usually consists of measures to help control signs and symptoms, reduce complications, and slow the progression of the disease. If your kidneys become severely damaged, you might need treatment for end-stage kidney disease.

DIALYSIS:

Dialysis is a procedure to remove waste products and excess fluid from the blood when the kidneys stop working properly. It often involves diverting blood to a machine to be cleaned.
There are 2 main types of dialysis:

- Haemodialysis involves diverting blood into an external machine, where it's filtered before being returned to the body
- Peritoneal dialysis involves pumping dialysis fluid into the space inside your abdomen (tummy) to draw out waste products from the blood passing through vessels lining the inside of the abdomen

<u>MUSCULAR AND SKELETAL SYSTEM AS SCAFFOLDS:</u>

Skeletal muscle architecture is one of the most important properties that determine a muscle's force and excursion capability. In the current review, basic architectural terms first are reviewed, and then specific examples relevant to upper extremity anatomy are presented. Specific examples of anatomic considerations required for surgical reconstruction after radial nerve palsy also are detailed. Together, these data show not only the wide variety of architectural designs in human muscles but the importance of considering architectural design when making surgical decisions.
The relationship between structure and function in skeletal muscle has been described and probed for more than a century. A classic study has elucidated the microscopic and ultrastructural properties of skeletal muscle fibers, yielding great insights into their function. However, less attention has been given to excellent and insightful studies of the macroscopic properties of skeletal muscle tissues dating back to the 1600s. This macroscopic arrangement of muscle fibers is known as a muscle's architecture.

Architecture:
The musculoskeletal system (locomotor system) is a human body system that provides our body with movement, stability, shape, and support. It is subdivided into two broad systems:
<u>Muscular system</u>, which includes all types of muscles in the body. Skeletal muscles, in particular, are the ones that act on the body joints to produce movements. Besides muscles, the muscular

system contains the tendons which attach the muscles to the bones.
Skeletal system, whose main component is the bone. Bones articulate with each other and form the joints, providing our bodies with a hard-core, yet mobile, skeleton. The integrity and function of the bones and joints are supported by the accessory structures of the skeletal system; articular cartilage, ligaments, and bursae.

Besides its main function to provide the body with stability and mobility, the musculoskeletal system has many other functions; the skeletal part plays an important role in other homeostatic functions such as storage of minerals (e.g., calcium) and hematopoiesis, while the muscular system stores most of the body's carbohydrates in the form of glycogen.

Mechanism:
The nervous system (your body's command center) controls your voluntary muscle movements. Voluntary muscles are ones you control intentionally. Some involve large muscle groups to do activities like jumping. Others use smaller movements, like pushing a button.
Movements happen when:
Our nervous system (brain and nerves) sends a message to activate your skeletal (voluntary) muscles. Our muscle fibers contract (tense up) in response to the message. When the muscle activates or bunches up, it pulls on the tendon. Tendons attach muscles to bones. The tendon pulls the bone, making it move. To relax the muscle, your nervous system sends another message. It triggers the muscles to relax or deactivate. The relaxed muscle releases tension, moving the bone to a resting position.
Hundreds of conditions can cause problems with the musculoskeletal system. They can affect the way you move, speak and interact with the world. Some of the most common causes of musculoskeletal pain and movement problems are:

- Aging

- Arthritis
- Back problems
- Cancer
- Congenital abnormalities
- Injuries
- Osteoporosis
- Muscular dystrophy

Everyone has pain in their muscles and joints from time to time. One of the most common musculoskeletal conditions is Osteoporosis. More than 60% of people in the United States have Osteoporosis at some point in their lives. Arthritis is also very common. More than 54 million adults in the U.S. have Muscular dystrophy. Most people recover from these disorders without long-term health problems.

BIO-ENGINEERING SOLUTIONS FOR MUSCULAR DYSTROPHY AND OSTEOPOROSIS :

Awareness is increasing that bone morbidity due to osteoporosis is a major complication of Duchenne muscular dystrophy (DMD) and its treatment and that it requires monitoring for early diagnosis and intervention to prevent clinically important sequelae.
The traditional method of fabricating 3D muscle constructs first developed more than 25 years ago involves casting myogenic cells within a cylindrically shaped collagen-I gel that is anchored at the ends to porous felts. In this system, cell-mediated gel compaction and remodeling result in the generation of uniaxial passive stress within the gel, which, in turn, promotes the fusion of myoblasts into myotubes and also myotube alignment. Alternatively, myoblasts, or mixtures of myogenic precursors and fibroblasts, can be cultured on laminin- or hydrogel-coated dishes until spontaneous contractions of formed myotubes detach the entire cell layer, allowing it to self-assemble into a cylindrical tissue construct attached at the ends to premade suture anchors.

Although cell alignment within 3D constructs is not required for the formation of contractile myotubes, it increases fusion efficiency while passive stress promotes both cell survival and myogenesis. In addition to collagen I, different natural hydrogels and their chemically modified derivatives can support the 3D growth and fusion of myogenic cells; the most functional results have been achieved using fibrin-based gels. Carefully optimizing the composition of the fibrin gel to enhance cell-matrix interactions as well as optimizing the starting cell population to improve myogenic fusion and SC maintenance and providing dynamic culture conditions to improve cell survival and maturation have enabled rodent skeletal muscle tissues to be engineered with contractile properties comparable to those of native muscle (e.g., twitch and tetanus-force amplitudes).

Rapid-prototyping techniques for hydrogel molding can be further used to vary local myofiber alignment and to design complex muscle structures, and advanced biomaterials can deliver angiogenic, myogenic, and pro-survival factors to cells in a spatiotemporally controlled fashion. In addition to using biomaterial scaffolds, scaffold-free muscle tissue constructs have been generated using magnetic fields that allow the controlled assembly of magnetically labeled cells, as well as thermo-responsive polymers that allow controlled cell detachment from culture surfaces.

Although hydrogels have been the dominant muscle-engineering scaffold in vitro, in vivo studies of muscle repair have mainly utilized acellular natural scaffolds, porous matrices made of degradable polymeric materials, or scaffold-free myoblast sheets.