Artificial Bladder

The human body contains many organs, which people subjectively divide in more or less complex ones. Even if the bladder seems to belong to the latter one, it is far more complex than we used to think and its complexity became clear during designing an artificial bladder. But before talking about a new artificial bladder, we will briefly review its anatomy and physiology, as well as the pathologies that could affect this organ, because it is necessary to characterize the profile of the patients that we target with our artificial device. Afterwards we will discuss the currently used approaches with their limitations and the promising field of tissue engineering. Finally, after all these considerations, the design of our artificial bladder will be shown, as well as its anticipated limitations and future improvements. In the final conclusion we will end with the underlying reasons for the decision of our model of an artificial bladder.

1. Anatomy and Physiology

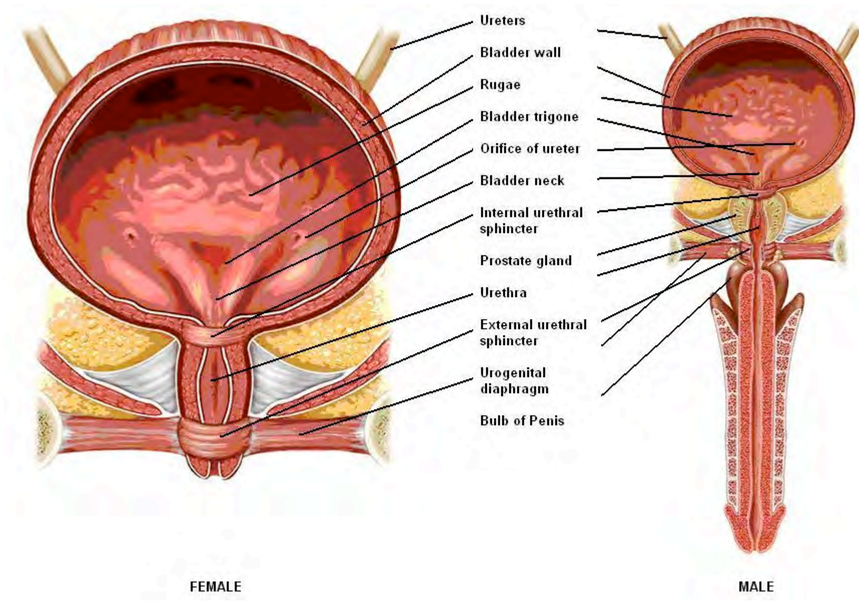


Figure 1 : Anatomy of Urinary Tract

The urinary bladder can be generally divided into two main parts: the body which is the major part where urine collection occurs, and the bladder neck which is a funnel shaped extension of the body. The triangular area above the bladder neck builds the so-called trigone. In the lowermost apex, the bladder neck opens into the posterior urethra (urethral orifice) and the entering of the two ureters (urethral orifice) into the bladder occurs in the uppermost apex of the trigone.

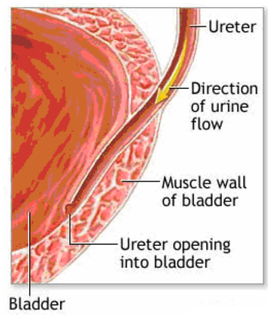


Figure 2 : Anatomy of Urinary Tract

Urine has its final composition when it leaves the kidney and is transported through the ureters into the bladder. This transport is done by peristaltic waves along the ureter which increases the pressure so that the region passing through the bladder wall opens and allows urine to flow into the bladder. But how does the bladder prevent backflow of urine to the kidney? The answer lies in a flap-like valve of mucous membrane that covers each urethral orifice. As the ureters enter the trigone, their distal ends courses through the bladder wall under an oblique angle (Figure 2). During the filling phase the increasing pressure compresses and closes the distal ends. As a consequence the bladder wall and the portion of the ureter which lies in it distend and become thinner. When it stretches, it is compressed against the detrusor backing thus allowing a continual flow of urine from the ureter into the bladder and preventing backflow.

The storage and voiding of urine is a part of the so called micturition. Before we will have a closer look at this process it is important to determine the bladder tissue (Figure 3). The bladder wall consists of four layers: the mucosa, submucosa, the detrusor muscle and the adventitia. The mucosa is divided into transitional epithelium and the lamina propria. The transitional epithelium is made of multiple layers of epithelial cells, which can contract and expand. The lamina propria is a thin layer of loose connective tissue which lies beneath the epithelium. The mucosa of the trigone is smooth whereas the mucosa of the rest of the bladder is folded to form rugae, which is a serie of ridges produced by folding of the bladderwall. The submucosa is a layer of dense irregular connective tissue that supports the mucosa and also contains blood vessels, lymphatic vessels and nerves. The detrusor muscle which is relaxed when the bladder becomes filled and contracts during voiding, continues with the internal sphincter, which surrounds the urethrals. This ring of smooth muscle fibers is controlled by the brain and is under automatic surveillance, whereas the external sphincter, which contains skeletal muscle fibers, is under voluntary control (Table 1). The two sphincters play a key role in the micturition process, which is described by cycles where the urinary bladder empties when it becomes filled. It consists of two phases: storage and emptying that requires a coordinated interaction between the bladder and the nervous system.

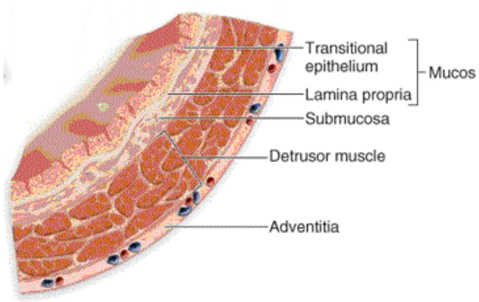


Figure 3 : Anatomy of Bladder wall

Characteristic	Internal Sphincter	External Sphincter
Type of muscle	Smooth	Skeletal
Nerve reaching the structure	Hypogastric	Pudendal
Nature of innervation	Automatic	Somatic

Table 1: Overview of the Urethral Sphincters

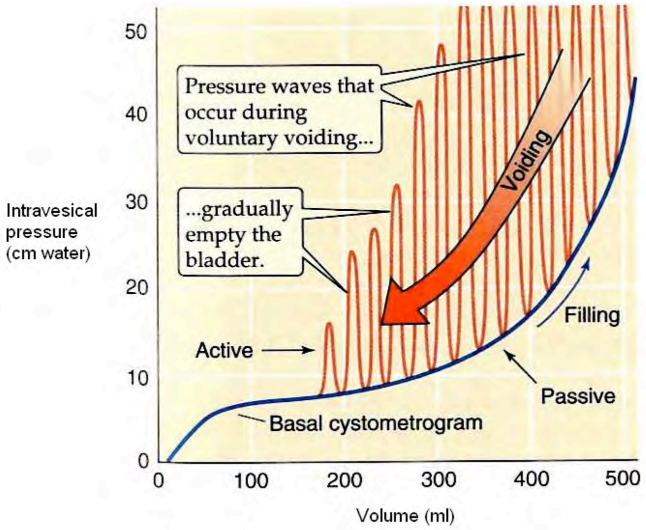


Figure 4: Cystometrogram

As urine accumulates, stretch receptors in the bladder send afferent signals to the brain through the pelvic nerves. These spinal reflexes causes an increase in the sympathetic inhibition of the bladder detrusor muscle which keeps the internal sphincter closed. The reflexes stimulate also the contraction of the external urethral sphincter by activating pudendal motor fibers. Both sphincters are therefore closed and urine can be accumulated in the bladder. When the amount of urine accumulated reach 200 ml, afferent impulses are transmitted to the brain, creating the urge to void. Then contractions of the detrusor muscle in the bladder wall start to appear and, as the filling process continues, becomes more urgent and frequent, thus initiating the voiding reflex (Figure 4). Visceral afferent impulses activate the micturition center of the dorsolateral pons, which signals the parasympathetic neurons to stimulate contractions of the detrusor muscle which leads to an opening of the internal sphincter. Finally, when the external sphincter is relaxed urine can flow out of the bladder.

If there is no urine in the bladder, the intravesicular pressure is about zero and 200-300 ml of urine can be collected without significant pressure change, because of the elasticity of the bladder (Figure 5). However, after the volume of urine accumulated reaches 300-400ml, the pressure rises rapidly and micturition waves occur. These waves describe a periodic acute increase of the bladder pressure, where the pressure peaks have different amplitudes. If the bladder is only partially filled these micturition contractions relay spontaneously, the detrusor muscle stops contracting and the pressure falls back to the baseline. But when the bladder becomes more and more filled the micturition contractions become more and more frequent and the urge to void increases.

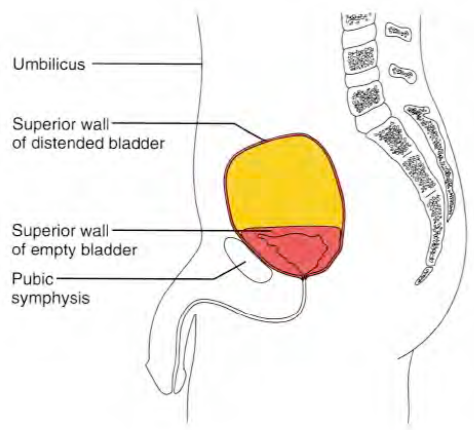


Figure 5: Bladder elasticity

2. Pathologies leading to the removal of the bladder

Many disorders can lead to a partial or complete dysfunction of the urinary bladder. Particularly, inflammation (cystis) is very common in young women and in older age groups of both sexes. Incontinence is another frequent health problem in elderly people and paraplegic. Nonetheless, these disorders are more disabling than lethal, whereas congenital anomalies and bladder cancer are more severe and can even lead to death.

In fact, bladder cancer is the ninth most frequent cancer in the world. There are different types and grades for this pathology. Small papillary and noninvasive carcinoma can usually be treated by a transurethral resection, whereas patients with multifocal bladder tumors and/or a high risk of recurrence are treated with a topical immunotherapy. This therapy consists of an intravesical installation of an attenuated strain of Mycobacterium tuberculosis called *Bacillus Calmette-Guérin*, which induces a local cell-mediated immune reaction that destroys tumor cells. If these treatments fail, or if the tumor has already invaded the muscularis propria, the bladder has to be removed by a surgical procedure, which is called cystectomy. In such cases, the bladder is often removed together with internal genital organs, such as the prostate gland and the seminal vesicle in males and the uterus and ovaries in females, depending on the severity and grade of the cancer.

Epidemiology of Bladder Cancer

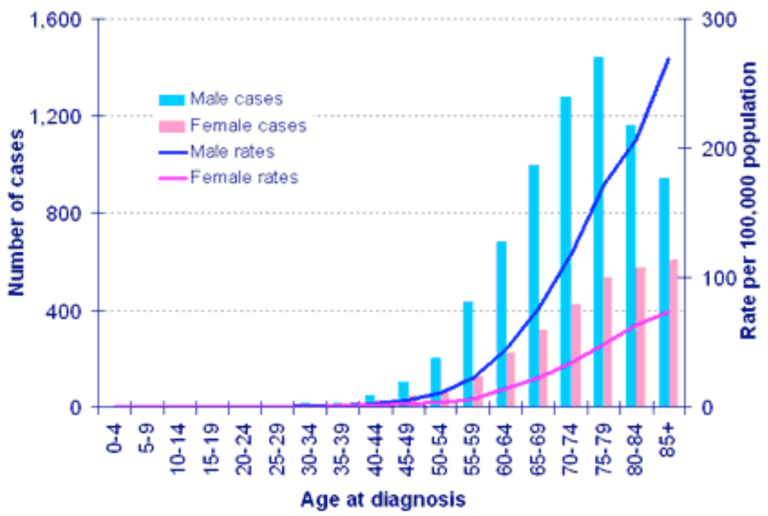


Figure 6 : Numbers of new cases and age specific incidence rates, by sex, bladder cancer, UK 2005

It is estimated that 357'000 bladder cancer cases occurred in 2002. This cancer is relatively common in developed countries, where 63% of all incident cases occur and is more common in men (77%) than in women (Figure 6) (Global Cancer Statistics 2002). Its incidence is very rare in people younger than 50, and it drastically increases with age. About 20-30% of bladder cancers are muscle-invasive and have to be treated by a radical cystectomy. So we estimate that about 90'000 patients worldwide would need a bladder reconstruction caused by cancer per year.

3. Current approaches and their limitations

Current approaches

Different approaches are currently used in order to reconstitute partially the function of the urinary bladder after cystectomy. The choice of urinary diversion depends on different factors, such as the medical history and the expectations of the patient, as well as on the experience and preferences of the surgeon.

The urine produced by the kidneys has to be collected and removed from the body. After a cystectomy, an ileal conduit (Figure 7) can be constructed by using a piece of the small bowel to carry the urine from the ureters to an opening in the abdominal wall (stroma), where the urine can be collected extra-corporally using an urostomy bag. This option can be modified by including an internal reservoir made of a piece of the small bowel, which is connected to the stroma. Urine should not leak as surgeons use a part of the bowel where there is naturally a valve. The urine can be drained by using a catheter through the opening.

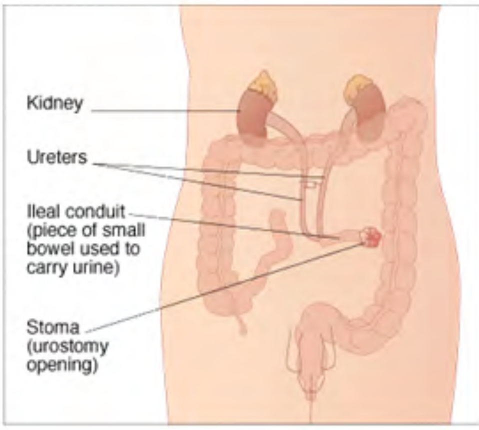


Figure 7: Ileal conduit

The most advanced technique is the bladder reconstruction (Figure 8). A part of the small bowel is used to create a pouch-like reservoir that is connected to the ureters and to the urethra, using the natural way of voiding. In order to pass urine in this case, the patients have to do a 'Valsalva manoeuvre'. This increases the internal pressure in the abdomen and leads to the voiding of the pouch.

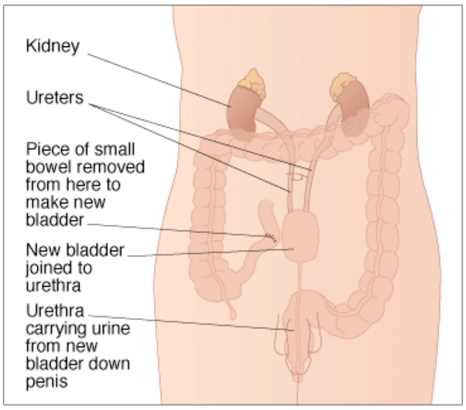


Figure 8: Bladder reconstruction

Liminations of the current approaches

It is obvious that these surgical interventions lead to complications, as the small bowel is placed in a highly unphysiological environment. The part of the small bowel that is used for the bladder reconstruction is continuing its secretory and absorptive functions. The Ileum and the colon secrete Na^+ and HCO_3 and reabsorb ammonia, H^+ and Cl^- when exposed to urine. This can lead to a hyperchloremic metabolic acidosis due to an excessive absorption of chloride and ammonia. Infections and renal stone formations are more frequent in patients with intestinal urinary reconstruction (Pow-Aang et al, Advancements in bladder replacement construction and continent urinary diversions have reduced treatment morbidity for patients facing cystectomy). Other complications are related to the removal of a part of the intestine, which can lead to diarrhea.

4. Other interesting approaches

Different approaches, using organic or synthetic materials, have been investigated as bladder substitutes but have usually failed because of mechanical, structural and biocompatibility problems. The synthetic materials usually induce mechanical failure and urinary stone formation, whereas the degradable materials provoke fibroblast deposition and a decrease in the reservoir volume. Other attempts using segments of stomach or bowels (autologous) are very common, but lead to many complications such as infections, increased mucus production, metabolic diseases, growth of abnormalities and carcinogenesis.

One way to avoid this kind of complications would be to use the native bladder tissue itself. However, the human organ donors available are very limited and the problems of tissue compatibility and rejection are still important. For these reasons, the bladder regeneration by tissue engineering seems to be a very attractive and promising approach and a lot of research is currently carried out in this field.

The different attempts for bladder regeneration can be categorized in three main groups: (1) the bladder autoaugmentation or detrusectomy, (2) the use of tissue template to induce regeneration and (3) the bladder bioengineering approach.

Bladder autoaugmentation

In the bladder autoaugmentation approach, the surgeon excises a part of the detrusor muscle leaving the bladder epithelium intact, thus creating an extensible bulge in the dome of the bladder. The main advantages of this method is that sutures or graft harvest are not required and the risks of infections and rejections are limited. However, it is only suitable for some specific cases, such as patients with low capacity high-pressure bladders and seems to lead to many complications.

Tissue template

Another approach uses graft framework or templates to induce regeneration of the bladder tissue. Some materials are known to have this property and they can be either biodegradable (such as polyvinyl sponges, polyglactin or collagen), alloplastic (such as polyethylene, PTFE or silicone rubber, which are used as temporary implants to allow regeneration and which are then removed) or organic (placenta, chemically treated pericardium, small intestine submucosa or acellular matrices). The alloplastic prostheses have many inconvenient, such as rejection, extrusion, calculus formation, shrinkage, urinary fistulae and peritonitis and have not been proved to be very efficient for regeneration. However, the biodegradable synthetic materials, despite their softness that make them hard to manipulate, show promising long-term results: re-epithelialisation and even smooth muscle regeneration.

With the placenta membrane, the results are very good too: complete regeneration of the bladder mucosa, presence of a normal lamina propria and ingrowth of bladder muscle, but the risks of rejection are much higher than with the synthetic materials.

Concerning the chemically treated pericardium, the epithelium successfully regenerated but not the smooth muscle layer.

The small intestinal submucosa, which is a collagen-based material, is obtained from the pig’s small intestine in which the tunica mucosa, the serosa and the tunica muscularis are removed, producing a thin graft that allows the regeneration of the three normal bladder layers: urothelium, smooth muscle and serosa, and even showed a contractile activity, due to the presence of new nerve fibers.

Finally, the acellular matrices, made of collagen and elastin and obtained from intestine, stomach or bladder, can induce complete mucosa and smooth muscle regeneration, as well partial innervations, leading back to truly functional bladder. These matrices have the advantage of not stimulating too much the host's immune system and not inducing scar formation.

Nonetheless, this approach still shows some mechanical, structural, functional or biocompatibility problems: permanent synthetic materials lead to mechanical failure and calculus formation and natural materials that are usually resorbable show graft contracture and resorption fairly due to the inflammatory response. In addition, this technique applies only for partial bladder regeneration.

Bioengineering approach

It is known that the bladder has the capacity to regenerate over free grafts by growing from the edges of the normal bladder towards the free graft and that the urothelium has a high reparative capacity. The tissue engineering approach uses these properties and can be decomposed in three main steps:

I. Urothelial and muscle autologous cells can be harvested from biopsies and expanded extensively in vitro (for urothelial cells we can obtain from 1 cm^2, 4200 cm^2 in 8 weeks).

II. Scaffold made of polyglycolic acid and poly-DL-lactide-co-glaycolide are designed to have the desired properties (shape, structure, porosity, rigidity, elasticity, degradation rate, …).

III. Cells are seeded onto these scaffolds: urothelial cells and muscle cells onto the inner and the outer surface respectively. The scaffolds with cells are then grown in culture and implanted in vivo to replace the native bladder.

Many experiments have shown that the harvested and expanded urothelial and muscle cells can attach to these artificial scaffolds in vitro and once implanted, could survive, proliferate and reorganize into a new bladder showing a spatial orientation and a normal histomorphology.

Some experiments were conducted in dogs, where the scientists showed that after the new-engineered bladder implantation, the dogs retrieved a bladder capacity of 95% of the initial volume and a compliance similar to that measured initially. The cellular organization was comparable to the normal one, with the presence of the three layers: urothelium, submucosa and muscle, as well as some neural structures. Even if others have obtained the same histological results with free grafts, the presence of cells seems to be necessary for satisfactory histomorphological and functional values. Moreover, the cell-free grafts they used in these previous studies were obtained by resection of less than half of the bladder, whereas with the bioengineering approach, the dogs underwent a trigone-sparring bladder removal (> 50% of the bladder removed).

Nonetheless, the cell-free grafts used as control in this present study on dogs showed a slight increase in volume (46% instead of 95% of the initial value), a loss of compliance, a shrinkage and the presence of fibroblasts and inflammatory cells. Furthermore, even if the urothelial layer was well developed, the graft was noticeably deficient for the muscular layer.

A company in the United States, named Tengion, is currently working on this technology and has recently completed its first Phase II clinical trial with its Neo-Bladder Augment for children with neurogenic bladder due to Spina Bifida and its enrolment for a second Phase II trial in patients with spinal cord injuries. This suggests that the bioengineering approach could be a very promising approach that could allow forming a new functional bladder, while limiting the complications present in other approaches.

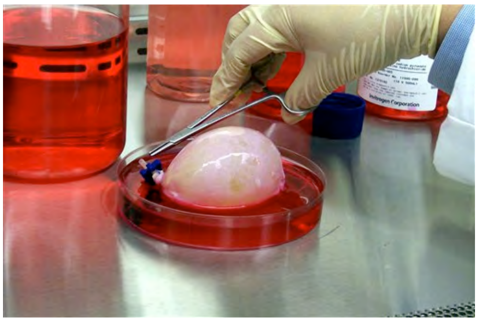


Figure 9: A neobladder seeded with cells

However, this technology is still in development and since the clinical trials have just started 2 years ago and it is not already on the market, we have too many unknowns about its potential success on bladder disease treatments.

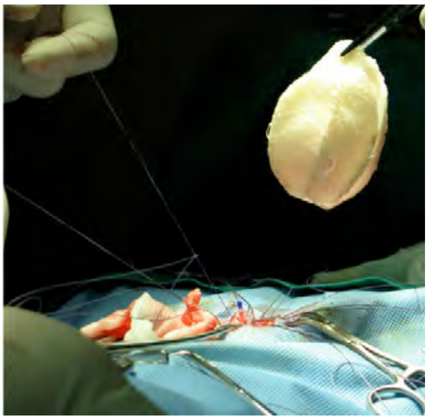


Figure 10: Application on a patient

5. Our model of an artificial bladder

Patients who have undergone a radical cystectomy are the main target group for our artificial bladder and our goal is to enhance their quality of life compared to other existing treatments. However, since this market represent a small number of patients, our device has to be as simple as possible and should not require too high development costs.

Requirements

To mimic as best as possible the original function of the bladder, our artificial bladder should have a capacity close to the natural bladder, should be placed at the original position in the lower abdomen using the natural way of voiding and the patient should be able to control the voiding process. Moreover, it should avoid backflow in the ureters, because otherwise it could damage the kidneys and should be fixed to prevent the stretching of the ureters.
According to these requirements, the artificial bladder must have 4 segments:

1) The bag - reservoir
2) Ureter & urethra connection tubes
3) Ureter Valves
4) Sphincter for the urethra

The main part is the bag, which acts as reservoir to retain urine before its voiding. It must be extensible at low pressure and resistant to external pressure.
All the components have to be impermeable and biocompatible and the major challenge is to find such materials that are stable and reliable when exposed to urine. Moreover, these materials shouldn't induce stone formation or infections. Silicone could be a possible solution: it is a soft material allowing volume changes that is commonly used for medical devices, because of its high biocompatibility and chemical inertia, which assure stability over long periods.

Device generalities

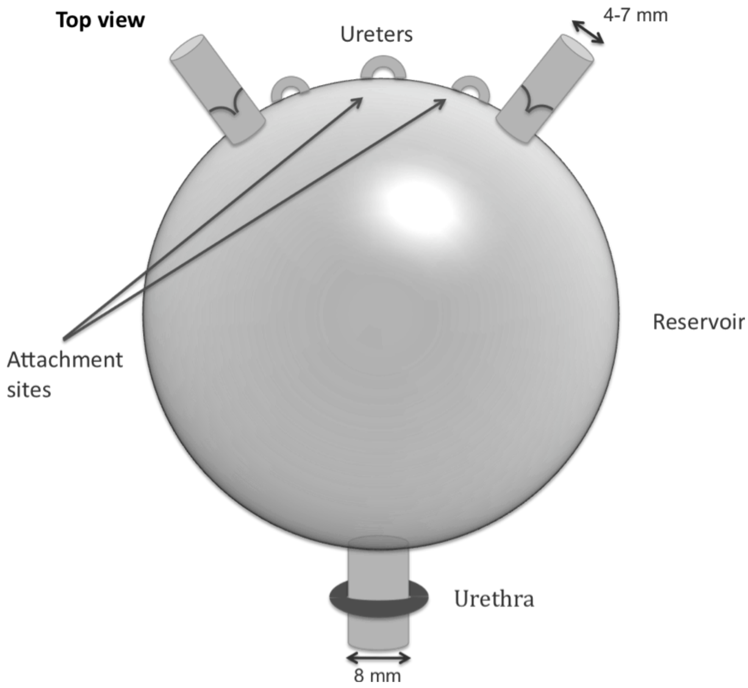
A normal bladder has a capacity of 400 to 600 ml, therefore to stay close to physiological values, we decided to make a 400 ml bladder reservoir. In general people drink about 1.5 l per day, but as we want to anticipate stone formation and infections, patient will have to drink more. Thus if they drink 2-2.5 l, they would have to urinate around 6 times a day.
The lifetime of our device should be between 5 and 10 years, and replacement will be easy for the surgeon because of the bladder location.

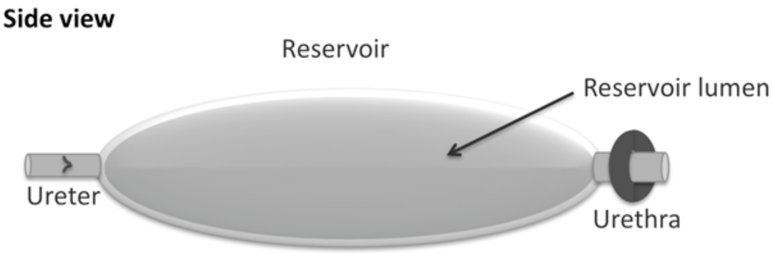
Design

Reservoir

The reservoir looks like a simple baloon that has a rugby-like shape, probably made of silicon and with a capacity of 400ml in its extended state. When the reservoir is voided, it looks like a wrinkled baloon, thus imitating the natural bladder.

There are three attachment sites on the upper part of the reservoir, helping the surgeon to attach the bladder to the surrounding tissues and preventing a displacement of the baldder and the stretch of the ureters.

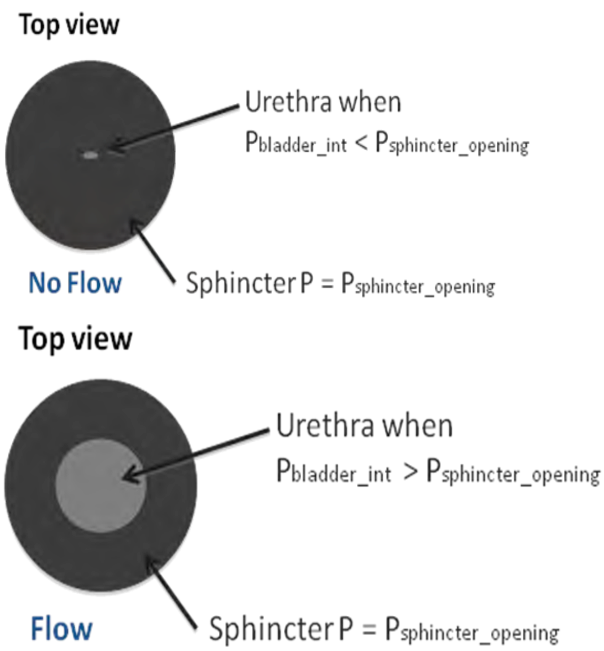




Sphincter

The sphincter is a ring made of an elastic material, isolated into a rigid tube, to avoid external forces acting on it. The ring has a constant internal pressure. In the resting state, its pressure is bigger than the internal pressure of the bladder, thus nothing will flow through.

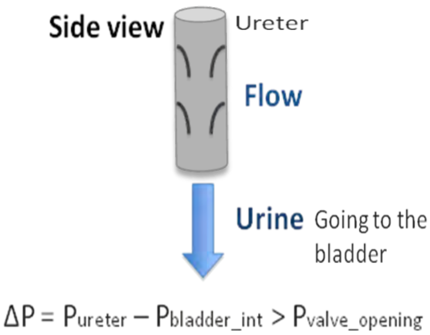
When the internal pressure of the bladder increase so that it becomes bigger than the pressure of the sphincter, the sphincter will open and let urea flow through the urethra. After the bladder voiding, its pressure will return to its normal value, and the pressure of the sphincter will afresh be higher than the bladder one, and will close again.



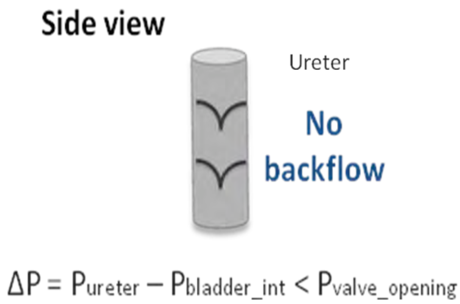
Valves

In natural ureters, three systems are present in series to avoid backflow to the kidneys. As kidneys are really important organs, it is necessary to protect them by avoiding backflow. In our system, we will use membrane valves and place two of them in series in order to decrease the probability of urea backflow.

The place for the income of the ureters into the reservoir was chosen on the top of the reservoir for different reasons: first of all, we want our device to be easily implantable for the surgeon, thus placing the artificial ureters closer to each other. We also don`t want them to disturb the application of an external force, as they would do if they were placed as in the natural bladder and finally, we don't want to add any hydrostatic pressure component.



For patient's comfort, it is important that these tubes are as fixed as possible, and this can be achieved by an upper part (between the artificial ureters) that is more rigid than the other part of the bag, by fixations sites.



The ureters tubes are made of a non deformable biocompatible material.

How it works

The reservoir is placed in the lower abdomen at the natural site of the bladder. The surrounding tissues exert some pressure on the reservoir, but in a resting state, the internal bladder pressure is close to 0 mmHg. The bladder can be filled with urine thanks to the peristaltic waves that increase the pressure in the ureters to about 15 mmHg.

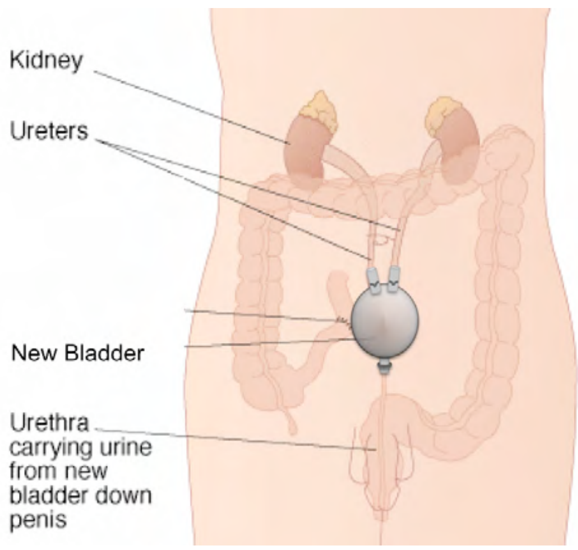
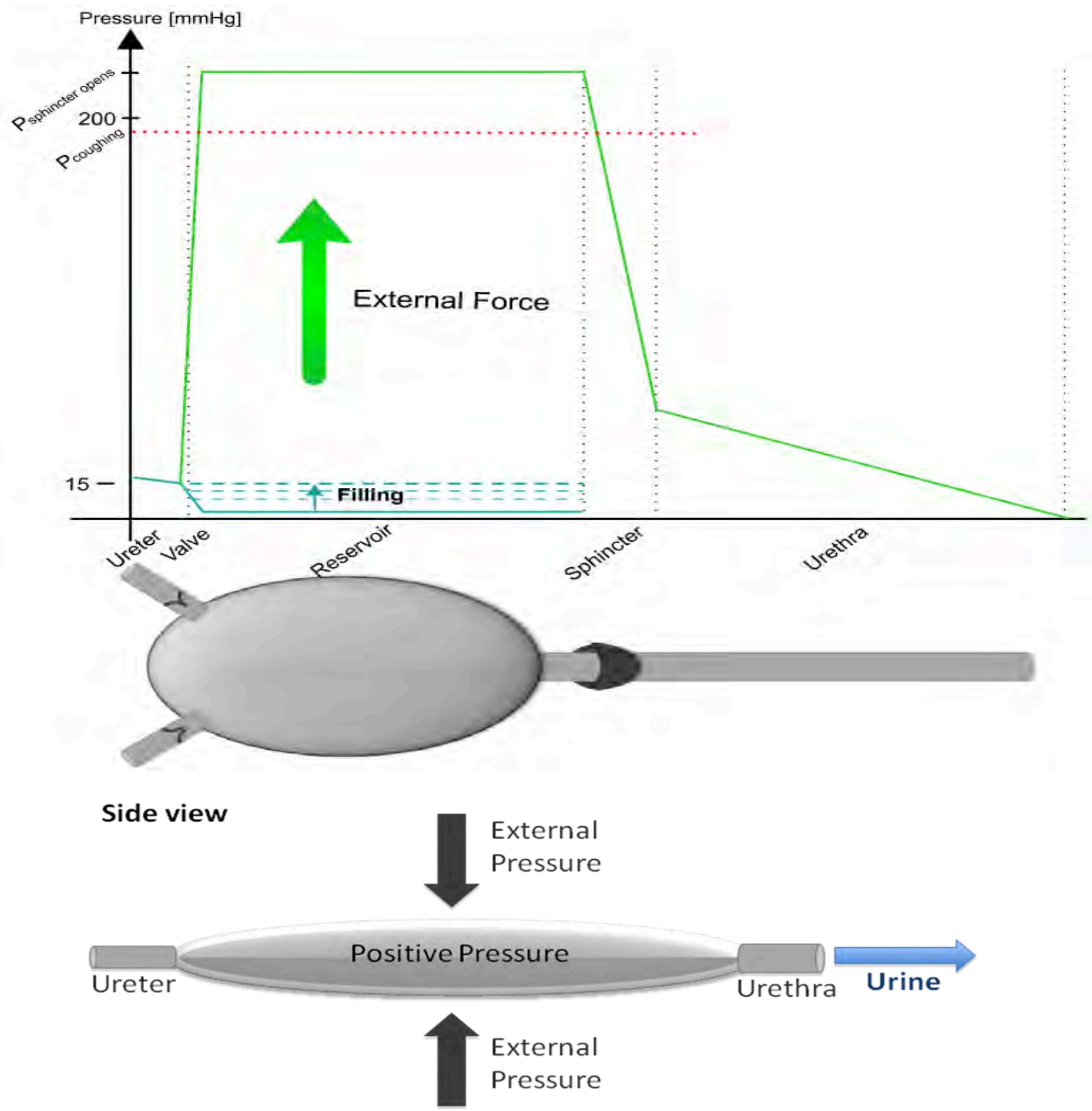


Figure 11: Placement of our device

If the pressure inside the reservoir increases up to 15 mmHg due to the filling, the urine flow from the kidneys is stopped which can be painful for the patient, remembering him that he needs to void it.

During special activities, such as lifting weights, retching, vomiting or coughing, the inter-abdominal and the bladder pressure can rise drastically up to 200 mmHg and to assure a certain quality of life, the patient shouldn't be incontinent during these activities. We thought to use a sphincter which opens only if the bladder pressure exceeds a certain limit that we defined to be slightly above 200 mmHg. By applying an external force on the patient's lower abdomen, the increased bladder pressure would open the sphincter and lead to the voiding of the reservoir.



However, obtaining a pressure of 200 mmHg seems to be difficult to achieve. If we assume that our reservoir is a sphere with a volume of 400 ml, the radius would be 4.57 cm, and the section area 66 cm^2. Therefore the external force needed for voiding would be around 175 N, which seems unrealistic. To reduce this force, several modifications can be made on our device. The first one is to decrease the pressure of the sphincter opening, but this will have an effect on the patient's life, because some urine leak could appear during sport or coughing. Thus, before doing sport the patient should void his bladder. Since the maximal pressure in the bladder during sport is 120 mmHg, another solution would be to decrease the bladder size, thus its area, and the opening pressure for the sphincter. Assuming a possible reasonable applied force of 70N, we can decrease the size of our bladder to a volume of 300ml and the pressure to 100mmHg. However, it will have a certain influence on the patient's life in the sense that he will have to go more often on toilets and has some leaks' risks in case of coughing.

It would be great to have an adaptable size of the bag, depending on the patient's morphology, but as seen previously, changing the size has an important influence on the applied needed force.

Being incontinent while coughing is not a satisfying solution and due to this limitation, it would be interesting to control the resistance of the sphincter. Ideally the patient, when he wants to urinate, could manually lower the resistance and hence wouldn't need to apply enormous forces on his lower abdomen. After voiding, the resistance should increase again assuring continence. A simple and interesting device exists for treating erectile dysfunctions: the AMS 3-piece inflatable penile prosthesis (Figure 12). It consists of a reservoir filled with a fluid (R), a pump (P) and cylinder (C). The tactile pump has a squeezing bulb, which can inflate the cylinders, and a deflation block allowing the fluid to flow back to the reservoir. By simply modifying the cylinders into a ring like structure, a manually controlled sphincter could be designed. The pump is usually inserted into the scrotum, but for female patients, it could also be inserted below the skin of the lower abdomen. This simple device, which is currently used in clinics, could overcome some limitations of our device with some small modifications. The patient could

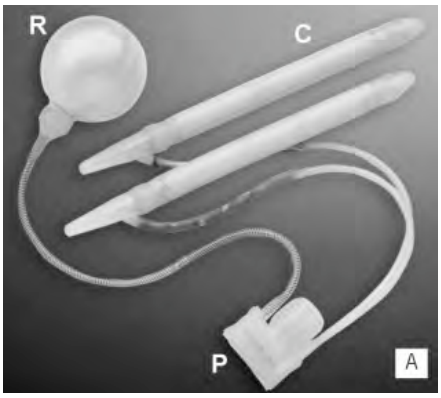
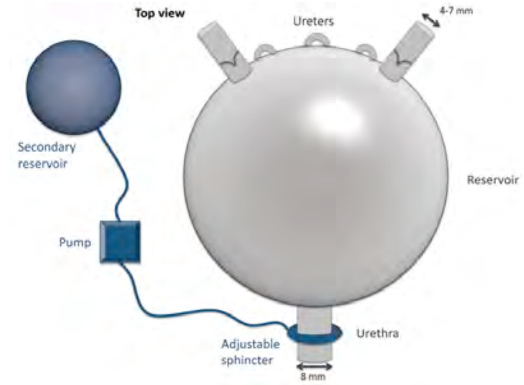
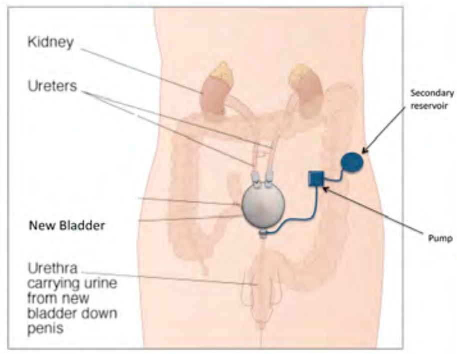


Figure 12: Penile prosthesis

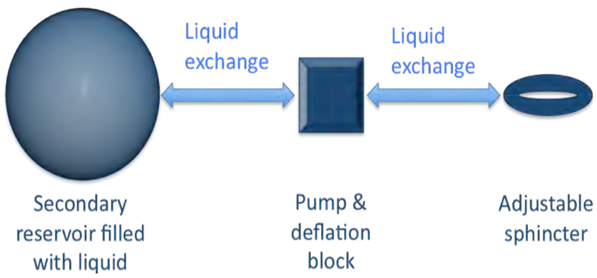
easily control the voiding process and continence can be assured during sports, coughing and all other activities.

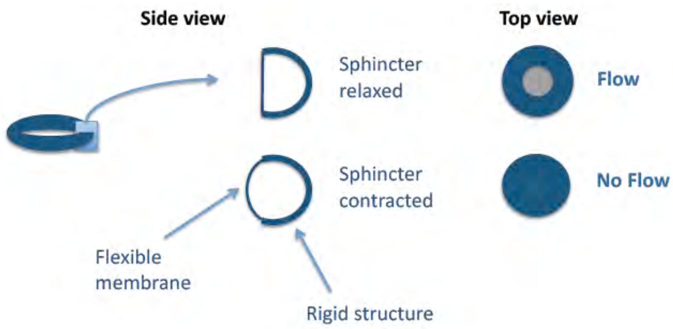
Modified device





The pictures above summarize the improved device including the mechanism for a regulation of the sphincter. The pump allows the patient an autonomous opening of the sphincter and therefore the control to pass urine. The mechanism of the controllable sphincter is based on an exchange of liquid. A pump situated between the adjustable sphincter and a secondary reservoir regulates the liquid exchange between the two components. In general the sphincter is contracted and prevents passing of urine through the urethra. In that case we have a higher pressure in the sphincter than in the reservoir. If the patient wants to empty the bladder he has to press the deflation block allowing the liquid flowing back to the reservoir caused by the pressure gradient. Therefore the sphincter is relaxed, allowing urine to pass through. To close the sphincter again he has to use the squeezing bulb pumping the liquid back to the sphincter.





Limitations of our device

If we consider a design for an artificial bladder it is important to discuss the influence and effect of urinary stone formation such as kidney and bladder stones.

Kidney stones also called renal calculi varying in size from pinhead to golf ball and their formation is caused by a crystallization of mineral residuals which are left behind in the kidney. Typical causes of urinary stone formation are a high level of urinary calcium (hypercalciuria), urinary oxalate (hyperorxaluria) or urinary uric acid (hyperuricosuria). Other causes could be e.g. insufficient production of urinary citrate, or inadequate water flowing through the kidneys. Physiological changes in the urinary pH for example due to infections could also lead to an increase in concentration of crystalloids.

Component	Mass
Uric acid	0.6g
Bicarbonate ions	1.2g
Creatinine	2.7g
Potassium ions	3.2g
Sodium ions	4.1g
Chloride ions	6.6g
Urea	25.5g

Table 2: Composition of Urine

Urine normally contains chemicals (Table 2) that help to prevent the formation of crystals and stones. Low levels of these inhibitors can contribute to the formation of kidney stones and in general about 90% of the stones of 4mm size or smaller can pass the ureters and urinary track spontaneous.

Problems with kidney stone formation in an artificial bladder can occur, when the stones are too big to pass the ureter valves and bloc them. In such cases, surgical interventions or medications are necessary, as for a natural bladder. The risk of a kidney stone formation is also increased when we have areas of stagnated urine flow like, for example, an accumulation of urine caused by the artificial valves. There are certain possibilities a patient with an artificial bladder has to consider to prevent this stone formation: a diet low in protein, nitrogen, sodium and a restriction of oxalate-rich foods as well as the drinking of 2-2.5 liters of water, or a drug treatment of thiazides, potassium citrate, magnesium citrate or allopurinol.

As well as for the formation of kidney stones, bladder stones are a result of waste products in urine that can also form crystals, therefore the same treatment methods used for the kidney stone prevention are possible and one possibility to avoid it, but also infections, would be to inject a drug cocktail just above the first valve.

Another aspect that has to be mentioned is how the patient recognizes the urge to void. The patient has to train himself to recognize and anticipate of the time to void, and this can be done by a special time-plan of drinking and eating behavior until he gets the routine.

Future improvements

To improve the patient's quality of life, an external control measuring the filling of the bladder could be added to our system in order to indicate to the patient via telemetry when he has to go to the toilet to empty it: for example, a simple capacitive distance sensor on two sides of reservoir wall. This improvement would increase the quality of life, but it would also increase the complexity of the device. However, this requires an energy source, which is time-limited, but that could sometimes be recharged from the outside using telemetry. We believe that an external control is not needed if the patient is well educated to its new medical device.

Finding a mean to allow an easier connection for the surgeon between the natural ureters and the tubes could also be something that can be developed later on.

Our device would be specific for people suffering from cancer who underwent a bladder removal. However, these patients are not the only one that need a new bladder, children with congenital anomalies may also need such devices. Such children can live but have, depending on the anomalies, a high risk to develop bladder cancer. Our device could be adapted to them, by reducing the device's dimensions.

6. Conclusion

Our first question at the beginning concerned the absence of artificial bladders on the market. Since the anatomy and system of the bladder don't seem to be too complex compared to other organs, where is the main barrier? Replacing an organ by an artificial substitute always requires doing a balance between the advantages for the patient and the risks that could occur. For example, for a patient suffering of incontinence, the risk of complications that could occur with an artificial bladder (problems during surgery, infection) could be much higher than the improvement of life standard.

Another important aspect is the cost combined with such organ replacement. Therefore, the components of the bladder have to be easily produced, the biomaterial used have to be cheap and the costs of the surgery to implant it should not be excessive. Finally, these costs have to be compared with the ones for existing treatments. Normally, they (e.g. in the case of incontinence) would be higher than existing treatments, which discourage artificial bladder development.

Moreover, at the moment there is also no known biomaterial that fulfils all necessary (e.g. biocompatible, no chemical interactions with urine, no cause of inflammation) and desirable characteristics (e.g. no urinary stone formation, no fatigue, low costs).From our point of view, that could be the reasons why there is no artificial bladder on the market today.

We therefore design our model under a specific constraint: as simple as possible. The simplicity of our model represents its main advantage: low costs and no external energy required. It could thus represent a very good opportunity (no often surgeries for charging batteries), even if some of its limitations have still to be overcome.

7. References

Figures

Figure1 :

http://www.waukesha.uwc.edu/lib/reserves/pdf/zillgitt/zoo234/diagrams/unit%204/ZOO%20234%20Urinary%20Bladder%20&%20Urethra%20Female.jpg

Figure 2 : http://www.nytimes.com/imagepages/2007/08/01/health/adam/19502Vesicoureteralreflux.html

Figure 3 : ttp://academic.kellogg.cc.mi.us/herbrandsonc/bio201_McKinley/Urinary%20System.htm

Figure 4 : Medical Physiology, 2nd edition, Walter F.Boron, Emile L. Boulpaep p.765

Figure 5 : Medical Physiology, 2nd edition, Walter F.Boron, Emile L. Boulpaep p.765

Figure 6 : http://info.cancerresearchuk.org/cancerstats/types/bladder/incidence/?a=5441

Figure 7 : www.cancerhelp.org.uk/help/default.asp?page=3169

Figure 8 : www.cancerhelp.org.uk/help/default.asp?page=3169

Figure 9 : http://www.cbsnews.com/images/2006/04/03/imageWX30304032243.jpg

Figure 10 : http://assets.bizjournals.com/story_image/122242-600-0-2.jpg

Table

Table 1: Medical Physiology, 2nd edition, Walter F.Boron, Emile L. Boulpaep S.764

Text sources

Medical Physiology, 2nd edition, Walter F.Boron, Emile L. Boulpaep, 2009

Medical Physiology, 11th edition, Guylan and Hall, 2006

Biomaterial Science, 2nd edition, Ratner, Hoffman, Schoen, Lemans

Tissue Engineering and Artificial Organs, 3rd edition, Bronzino,2006

Pathologic basis of Disease, 7th edition, Kumar, Abbas, Fausto, 2005, Elsevier Saunders

R.Keller et al, Repetitorium Chirurgie, Elsevier, 2007, p.446

Iqbal, A study of intragastric and intravesicular pressure changes during rest, coughing, weight lifting, retching, and vomiting, Surg Endosc (2008) 22:2571–2575

“Stones in the Urinary Tract”, Abbas www.aku.edu

“Tissue-Engineered Autologous Bladders: New Possibilities for Cystoplasty”, by Kropp, Zwischenberger, 2006 Nature

"Long-term durability, tissue regeneration and neo-organ growth during skeletal maturation with a neo-bladder augmentation construct", by Jayo, Jain, Ludlow, Payne, Wagner, Bertram, 2008, Future Medicine

"Bladder regeneration: between the idea and reality", Shokeir, 2002 , BJU International

"De novo reconstitution of a functional mammalian urinary bladder by tissue engineering", by Oberpenning, Meng, Yoo, Atala, 1998 Nature

"Bladder regeneration by tissue engineering", by Atala, 2001, BJU International

http://tengion.com/technology/platform.cfm

http://www.urostonecenter.com/anatomy.asp

http://physrev.physiology.org/cgi/content/full/84/3/935

http://anestit.unipa.it/esiait/esiaing/0397_01ing.htm