Urinary Valve and Delivery Device for Primary Vesicoureteral Reflux

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Abstract

Vesicoureteral reflux (VUR) is a condition where urine flows out of the bladder into the ureters, typically due to anatomical deformity of the vesicoureteral junction or bladder muscle weakness. Over time, this leads to recurrent urinary tract infections and calcification of the renal calyces. The only current treatment options are limited to antibiotics, overtime leading to resistance or surgical reconstruction of the junction, requiring a hospital stay and posing the general risks associated with surgery. We have developed a less-invasive approach to correct VUR using a novel hydrogel to support the existing valve. The hydrogel will be placed utilizing guidewire entry through the urethra where a designed encapsulation will deliver the hydrogel to the ureter. The pH testing done has determined the hydrogel will be able to withstand the range of pH present in the ureters. Verification testing that include simulations to observe appropriate flow rates, cytotoxicity and biodegradability to verify safe usage of the valve in the body, and delivery testing to ensure safe inserting of the valve, were all performed. Due to a lack of funding, cytotoxicity testing could not be concluded. Degradation of the valve by DMSO was observed, as hypothesized. Verification of the delivery mechanism was successful, as it demonstrated full ejection of the valve into place.

Introduction

Primary vesicoureteral reflux (VUR) is a condition in children, and occasionally adults where urine flows up out of the bladder up into the ureters, and in some cases, the kidney [1]. An estimated third of children with VUR experience recurring urinary tract infections (UTIs) [2]. The patient has an abnormal ureter, which makes the vesicoureteral junction not close properly [3]. In most children, as they outgrow the condition as the valve can close better. It affects approximately 1-2% of children [4].

VUR is graded on a scale of 1 to 5, where 1 is the least severe [1]. As the grade increases, urine flows further up the ureter and the ureter increases in size. The enlarged ureter results in an inadequate closure of the ureterovesical junction. Currently, for the higher grades of VUR, there are several surgical procedures, including open surgery, laparoscopic surgery, and endoscopic surgery [2].

The goal of this project was to design an implantable device that supports normal urine flow that would be effective at treating higher grades of VUR that would otherwise require surgery. The problem statement revolved around designing a device to be used in an outpatient procedure to treat primary VUR in adults or children who would otherwise require surgery with a one-way valve delivery system.

Design Inputs

The team defined the following requirements in which the device must obey:

1.The valve must be able to support the range of pHs present in urine(pH 5-7). [5]
2.The valve must be able to support normal urine flow into bladder by not moving due to flow rates up to 20mL/hr and intra-abdominal pressures up to 20mmHg. [6][7]
3.The valve must be biocompatible, with a reactivity less than or equal to 2 and cell death less than 30%. [8]
4.The delivery device must be able to range in length from 2-30cm long in order to reach the vesicoureteral junction through urethras of varying lengths. [9]
5.The delivery device must be less than 3mm in diameter in order to fit into the urethra. [10]
6.The delivery device must be able to place the valve correctly and separated from the valve for removal, as this is the function of the device.
7.The delivery device must be biocompatible. [11]

Design Solution

The valve design utilizes a novel PyKC hydrogel. The hydrogel material is made of protein polymers [1]. This material was selected because, according to literature, it is water insoluble and can withstand pHs ranging from 4-8, as what is common in urine. It also degrades when exposed to dimethyl sulfoxide, which is approved by the FDA for use in the bladder. As seen in Figure 1, the hole in the center is for the guidewire to go through the hydrogel. The hydrogel itself would be available in multiple diameters, depending on the patient's ureter and the extent of primary VUR.

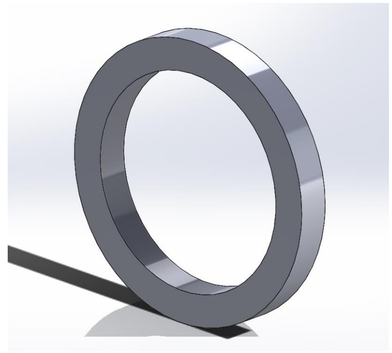

Figure 1: SolidWorks drawing of hydrogel valve

The designed delivery mechanism is based on the placement of a ureteral stent (Figure 2). A guidewire will be inserted into the urethra and through the bladder to locate the affected ureter. The hydrogel-filled, 3-D printed, encapsulation device and pusher will be fed along the guidewire until reaching the correct position. At this point the pusher will push the hydrogel valve into place. The guidewire, pusher, and encapsulation device will be removed, leaving only the valve behind. The 3-D printed component would be printed as polyvinyl chloride (PVC), as it is sterilizable and already is used in a variety of medical applications.

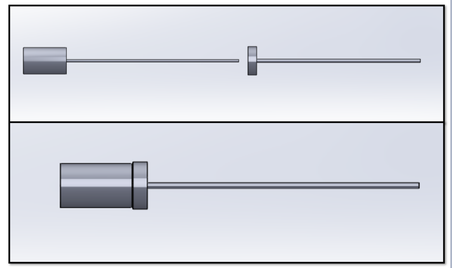

Figure 2: SolidWorks drawing of delivery mechanism

Testing

Verification and validation tests determined if the designed device met previously defined requirements. One of the valve requirements was that it must be able to support a pH range of 4 to 8 that is present in the urine. This was tested by creating a solution of water, baking soda and hydrochloric acid and varying the amount of each component depending on whether it was a basic or acidic solution. The hydrogels were placed in the solution and soaked for 7 days to observe whether degradation occurred. The hydrogel was also tested for cytotoxicity where a cell culture was done and suspension cells were placed with the hydrogel and left for 5 days. This test was inconclusive as cell death occurred due to the cultures being overcrowded. Material testing was also done to observe the behavior of the hydrogel. This involved soaking the hydrogel in saline for 24 hours then indenting the sample with a fixed displacement of 15 micrometers for 30 seconds. This was done four times to obtain four samples. Values obtained from this testing were used to calculate the diffusion coefficient and intrinsic permeability. These values were imported into ANSYS, where a valve-ureter simulation showed the valve would not move due to urine flow or intra abdominal pressure. To test the delivery mechanism, Jello was used in place of the hydrogel since the properties were similar. A known value of jello was inserted into the catheter and then implanted into pig bladders. The testing was successful since all the contents of the jello remained in the bladder and none was left in the catheter.

Conclusions

The goal of this project was to design a device that would treat VUR through a minimally invasive procedure. Current treatments were analyzed and observed to be costly and posed many risks that are associated with surgery. This led to the group's brainstorming of designing a valve with a catheter delivery mechanism, that would be placed in the ureter and overtime correct VUR. A hydrogel was constructed and tested in different pH settings that would particularly be found in the urine and was found to be able to withstand the range of pH. The delivery mechanism involved designing a catheter-type device that was found safe and performed as expected. As for the cytotoxicity testing, a conclusion could not be made on how the device would interact with the cells in the body since lack of funding was available. Degradation of the valve was also tested by saturating the hydrogel with DMSO that was observed to break down the hydrogel. Simulations were conducted to observe the effects of different flow rates on the hydrogel, and minimal movement was seen. The overall results of this experiment were as expected except for the cytotoxicity testing. We can conclude that once the device is fully biologically evaluated, the hydrogel valve and catheter delivery mechanism can be used as a new approach to treating VUR. This not only reduces the patient's recovery time, but it is efficient and not as costly as compared to current treatments.

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