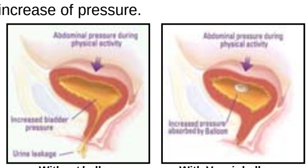
ANALYSIS OF SEDIMENT FORMATION ON LONG-TERM INDWELLING FREE-FLOATING INTRAVESICAL BALLOONS FOR THE TREATMENT OF SUI FROM TWO MULTICENTER RANDOMIZED CONTROLLED CLINICAL STUDIES

Stefan De Wachter[1], JJ Wyndaele[1], Eric Rovner[2], Karny Jacoby[3] , Roger Dmochowski[4], Giovanni Tommaselli[5], Susan Kalota[6], Gommert van Koeveringe[7]

1. University of Antwerp, 2. Medical University of South Carolina, 3. Urology Northwest, 4. Vanderbilt University, 5. Universita Degli Studi di Napoli "Fredico II", 6. Urology Associates of Southern AZ, 7. Maastricht University Medical Centre

Introduction

- **A novel free floating, non-occlusive, compliant intravesical balloon** filled with compressible gas has been evaluated in US and European multi-center randomized controlled clinical trials for the treatment of SUI. The balloon aims to reduce transient spikes in intravesical pressure that are common to all forms of SUI, regardless of their etiology.
- **Abdominal pressure transients are strongly related to leakage** associated with stress urinary incontinence. When an incontinent patient laughs, coughs, or sneezes, for example, abdominal muscles tighten and cause an increase in abdominal pressure. This abdominal pressure in turn, presses down on the urinary bladder causing a corresponding increase in intravesical pressure. If the intravesical pressure exceeds the urethral closure pressure then leakage occurs
- **Fluids are effectively non-compressible, but gases are compressible**. The behavior of a gas can be described by Boyle's Law: $P_1V_1 = P_2V_2$. Using this derivative of the Ideal Gas Law as a reference, consider that in response to a pressure transient, P1→P2→P1, an air-filled balloon will momentarily contract to a new smaller volume, V2. This contraction has a time constant that is proportional to the volume of air within the balloon, thus slowing the rate of increase of pressure.



Without balloon   With Vesair balloon

- **Applying Pressure Attenuation Technology to the Bladder**. With the addition of an air-filled balloon to the bladder, the intravesical pressure increase is dampened or attenuated. This limits the rate of pressure increase in the bladder, and for short events, limits the maximum pressure that will occur in the bladder associated with pressure events. Micturition is driven by sustained pressure, it should not be affected by the presence of the balloon.

Background

- **Encrustation is a concern with any intravesical device**, as the chemical constituents of the urine combine with the device to produce a matrix for the growth of stones. This formation may impact the efficacy of the device or result in stones dislodging from the device and becoming obstructive.

Figure 1: Section of encrustation from the region of the stent residing in the bladder: (a) stent resident for 58 days [1]

Figure 2: Section of encrustation on stent residing bladder for 58 days[2]

- **Two previous prospective, randomized, single blind, multicenter studies** assessed the safety and efficacy of this intravesical therapy on two different patient populations.[3, 4] Balloons from theses clinical studies were analyzed after removal from the patient to evaluate the formation of calcium oxalate and its impact to the efficacy of the device or the potential for stone formation.
- In Study 1, the protocol indicated that the balloons were intended for removal and replacement every 90 days. In Study 2, the protocol indicated that the balloons were intended to remain indwelling for up to one year.

Materials and Methodology

This study evaluated a total of 635 balloons removed from patients from two separate clinical studies.

Materials and Methodology (cont'd)

The Vesair ® Balloon

- **The balloon is thin and has a low mass**. It is constructed of polyurethane film - a material with a long history of biocompatibility, including use in the urinary tract. A one-way valve seals the balloon after filling with air.
- **The buoyancy of the balloon makes it inherently non-occlusive**. Since it is free-floating and not anchored in any way, it will naturally float at the top of the bladder.
- **Insertion Device**. The balloon is inserted deflated, inside the tip of a lubricated catheter-like 18F inserter. It is inflated once it is inside the bladder, and released.

3A - STUDY 1

3B - STUDY 2

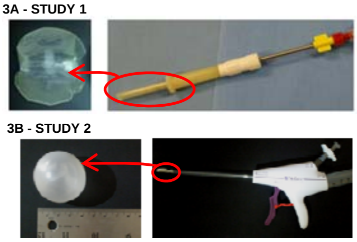
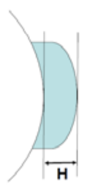


Figure 3: Balloon and delivery system

- **The balloons were removed transurethrally under direct visualization** using a custom optical grasper and placed in a specimen collection mailer and sent to a central location for analysis. All balloons were retained after analysis. The balloons were analysed by visual inspection for sediment using a 10-point scale ranging from 0 (0 to 0.1mm), 1 (0.1mm – 1.49mm), 2 (1.5mm to 2.49mm) up 10 (>9.5mm). For each device, the thickest deposit was measured at its thickest point.



H (mm)	Score
0 - 0.1	0
0.1-1.49	1
1.5-2.49	2
2.5 - 3.49	3
3.5 - 4.49	4
4.5 - 5.49	5
5.5 - 6.49	6
6.5 - 7.49	7
7.5 - 8.49	8
8.5 - 9.49	9
> 9.5	10

Figure 4: Scoring of sediment formation on balloon

- 539 balloons were from 159 patients in Study 1, which used a seamed pressure-attenuation balloon with a valve welded into the seam (Figure 3A) that was filled with 15cc of air.
- 96 balloons were from 75 patients in Study 2, which used a seamless Vesair pressure-attenuation balloon with a valve welded to a small fill port (Figure 3B) that was filled with 30cc of air.

Results

Study 1

482 (89.4%) of the balloons in Study 1 had no measurable sediment formation (Score =0). 33 had a score of 1, 15 had a score of 2, four had a score of 3 and three had a score of 4. All sediment for balloons with a score greater than 1 was located at the valve/seam interface.

Figure 5: Deposit Score Per Balloon, 10 Point Scale
539 balloons from 159 patients

Figure 6: Sediment scoring samples – Study 1

Results (cont'd)

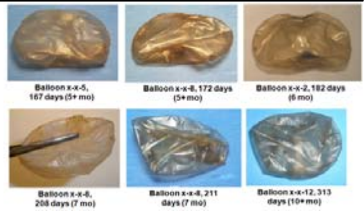


Figure 7: Representative samples – Study 1

Study 2

89 (96%) of the balloons in Study 2 had no measurable sediment formation (Score = 0.) The remaining three balloons had a score of 1.

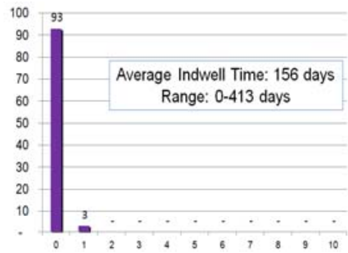


Figure 8: Deposit Score Per Balloon, 10 Point Scale
96 balloons from 75 patients

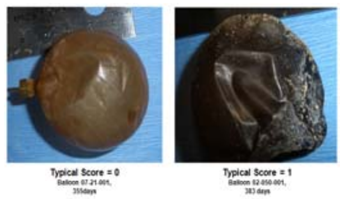


Figure 9: Sediment formation on balloon – Study 2

Figure 10: Representative samples – Study 2

Overall, in both studies:

- Any sediment formation that was measurable on the devices did not affect the device functionality and did not result in any obstructive issues.
- No patients had "stones" that were consciously passed or became obstructive.
- Representative samples of sediment from balloons were determined to be calcium oxalate by SEM Analysis.

Discussion

The Vesair Balloon is unlike other urological devices that remain in the urinary tract for extended periods of time. It is highly buoyant and floats at the top of the bladder, and moves continually as the patient moves, and contracts and expands with changes in intravesical pressure. Sediment formation was much less than expected, and the balloon design changes implemented in Study 2 further reduced sediment formation.

Conclusion

The Vesair Balloon is remarkably free of significant mineral deposit. Further study is required to better understand which of these factors resulted in the reduction of sediment formation.

References

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