



Meet Our Presenters:



Dr. Sia Daneshmand: Dr. Daneshmand earned his medical degree from University of California Davis and completed his residency at the University of Southern California. He was recruited to USC Institute of Urology in 2010 as the director of neurologic oncology. His main interests include bladder cancer, advanced kidney cancer and testicular cancer. And he has extensive experience in urinary diversion and reconstruction following surgical removal of the bladder.



Rick Bangs: Rick is an active patient advocate with BCAN and serves on the SWOG executive advisory committee. He's an IT and marketing professional and serves in several panels like the National Cancer Institute and the National Comprehensive Cancer Network, bladder and penile cancer panel. And also the ASCO, American Society of Clinical Oncology guideline committee. He's a bladder and prostate cancer survivor. And in 2006 received his neobladder.



Lydia Saravis: Lydia received her orthotopic neobladder in 2015. Since then, she's been a very active volunteer as a patient advocate, working with BCAN Survivor To Survivor Program and Imerman Angels. In 2017, she founded the neobladder support group and created a forum and provide support for individuals who have had neobladder surgery and their caregivers.

Dr. Sia Daneshmand:

So in USC, when we see patients, every patient undergoing radical cystectomy, is at least considered for orthotopic diversion, by the way, just the term orthotopic diversion means orthotopic means in the same place. It basically refers to a neobladder. There are some contraindications and we'll go through this. Next slide.

So this is a large database that looks at the likelihood of patients receiving orthotopic diversion. This is, again, a nationwide data base.

So the chance of you receiving a neobladder is higher if you're male, higher educational level, because you're doing your research and year of surgery, and whether this is done at an academic center and at National Cancer Institute designated cancer center, and of course, high volume providers who do more of this surgery.

Unfortunately, when you look also at the trends, now this is from 2004 to 2013. We presented this data at one of our national meetings a couple of years ago. You can see the number of continent diversions where the percentage is unfortunately going down instead of going up.

There are numerous reasons for this, most of which are guesses, but if you see the last one from 2004, about 17.6% of patients received a neobladder and in 2013, only 11.8%, this is national data. So looking across the US it looks very, very different at USC where 80% of age 75 to 80% of patients are receiving a neobladder.

Urinary Diversion at University of Southern California (USC)

Orthotopic diversion is arguably the gold standard

Every patient undergoing radical cystectomy is considered for an orthotopic diversion, except when one or more contraindications apply.



SEER Data

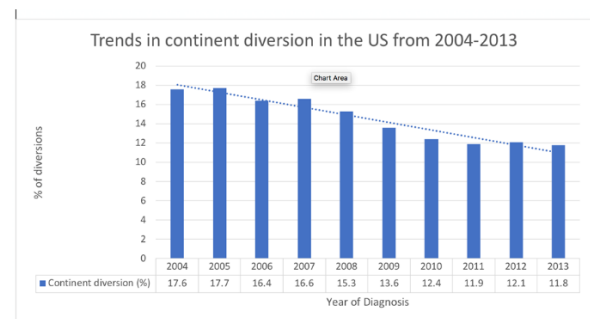
Likelihood of continent diversion: (multivariate analysis)

Inversely associated with

- older age
- African American race
- higher comorbidity index

Directly associated with

- male sex
- higher education level
- year of surgery
- academic and NCI-designated cancer centers
- high-volume providers



Form the National Cancer Database (NCDB)

Dr. Sia Daneshmand:

What are the actual contraindications or what are the reasons we cannot do a neobladder? If you have bad renal function, kidney function, you can just go through that, that's definitely one by one. If you have liver disease, compromise intestinal function, if you have a cancer right at the urethral margin where we take the bladder, if there is some mental impairment or some issues with hand function or preexisting

incontinence, we're not going to make that better with a neobladder, usually that gets worse.

Next line. Excellent. And radiation definitely increases our complication rates. But one thing that's important is that age is not a contraindication, at least not at USC. Next. So what are the factors that influence choice? Surgical training, where your surgeon trained and the influences of their mentors.

Most urology residents who are graduating from their training programs don't get enough experience doing neobladders. So it's important to know where you're at and what you're being offered based on the conversation.

So in 2003, again, this is old data, but it hasn't really changed much. Graduating chief residents performed a median of only three continent diversion. That's just not enough.

Our graduating chief residents each get probably 30 to 40 neobladders so

you can see the differences here when they get out there, their views on doing these are going to be very, very different. And only 30% of the programs are performing more than 20 urinary diversions during their training. And of course, management of complications is key. The more experience you have, the more you know how to manage these complications.

Contraindications for Orthotopic Neobladder

- Compromised renal function (Cr >1.8)
 - Severe hepatic dysfunction
 - Compromised intestinal function
 - Positive urethral margin
 - Mental impairment
 - Pre-existing incontinence
 - Pelvic radiation (increased complications)
 - Recurrent urethral stricture disease
- **AGE NOT CONTRAINDICATION!!**



Factors influencing choice

- Surgical training
- Most urology residents get insufficient experience with continent diversion during their residency
- In 2003, the **graduating chief residents** performed a median of **3 continent urinary diversion**.
- Only 30% of residency programs perform more than 20 urinary diversions during their training.
- Management of complications



Dr. Sia Daneshmand:

So I looked at, what about patient choice? You give them the three options. How many times are patients actually choosing their own? I looked at this a while ago, these were my own patients. They were 149 patients eligible for continent urinary diversion. There were only nine patients or 6% who chose to undergo an incontinence urinary diversion. So meaning it was a conduit for personal reasons.

Meaning we offered them a neobladder, but they preferred to have an ileal conduit for personal reasons. And this makes sense to us. But again, it all depends on how you present the options to the patient.

Our view is that proper patient selection, thorough standardized preoperative counseling can result in a higher rates of continence urinary diversion. I go back and forth again between the words orthotopic neobladder, continence urinary diversion, which also includes the continent cutaneous diversion, the diversion that you catheterize through the belly button or other cutaneous stoma there on the skin. Next.

So what are the reasons not to perform continent diversions? These are quotes used from what I've heard over the years. "The patient is too old." Again, I told you age in and of itself is not a contraindication. "Neobladders have more complication rates." Not true, at least not in our center and not at many other centers. So it depends on where you're talking about. "You will be leaking." The answer is yes, you will. But it depends again on how much and where and how and I think you need to quantify that.

"You'll have more infections with a neobladder," maybe true in the first 30 days, those are treated with antibiotics and certainly long term, you don't have more infections than you do with other types of diversion. "You need to catheterize yourself." True, but again, you need to quantify that. Only 15% of male patients will need to cap themselves. And we'll get into this a little bit later. "An ileal conduit is simpler a much shorter operation." Well, it is simpler. but again, for whom? "Much shorter." well at our



Factors influencing the choice of urinary diversion in patients undergoing radical cystectomy

Matt S. Ashley and Siamak Daneshmand

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Accepted for publication 6 November 2009

- Of the **149 patients** eligible for a CUD, **only nine (6%)** chose to undergo ICUD for **personal reasons**
- Proper patient selection and thorough, standardized preoperative counselling result in a higher rate of CUD

Reasons not to perform continent diversion

- "Patient too old"
- "Neobladder have more complication rates"
- "You will be leaking"
- "You will have more infections"
- "You will need to catheterize yourself"
- "Ileal conduit is simpler and much shorter operation"



center it's only about 40 minutes shorter because we just do so many neobladders, but that may not be true at other centers.

Dr. Sia Daneshmand:

Complications. Again, many are worried that if they have a neobladder, there are more complications. There are a number of publications showing early complications are actually not increased in continent diversion. Yet it's probably the number one reason cited to patients not to perform a continent diversion. Next slide. How about time and cost? It does definitely require resurgent time in the operating room and during the follow-up period there's lots more sort of discussion about what needs to be done. There's very poor reimbursement to the surgeons.

Complications

- Number of publications showing that early complications are not increased in continent diversion.
- Yet probably #1 reason cited to patients not to perform continent diversion.



Time/Cost:

- Continent diversion requires more physician time in the OR and during the follow-up period
- Poor reimbursement
- Strong financial **disincentive** for urologists to perform this more complicated procedure.



So there's a financial disincentive for urologist to perform these more complicated procedures. So at the end of the day, surgeons are also motivated by certain financial incentives as well. And if the patient doesn't care where the patient that the surgeon is going to choose the simpler one. Patient one wanted an ileal conduit, I think we went through that. While there may be not a consensus on improves quality of life, many patients and providers still consider continent diversion to be at least the more attractive option in many of the quality of life studies.

In many patients, this is a very important point. Many patients will actually avoid a cystectomy altogether because they've been told they need a stoma and they don't want to live with a stoma, so then they'll avoid the cystectomy and unfortunately their disease progresses. So on the topic of continence in orthotopic urinary diversion in the elderly, we looked at this in older patients looking at daytime continence, don't worry about the numbers, but just to show the both... Here it is, there's no significant association between age and daytime continence. And also when you look at nighttime continence, this is again, male patients. There was no significant association again between age and

Patient/surgeon personal views:

- "Patient wanted an ileal conduit"
- While there may not be a consensus on improvement in quality of life, most patients and many providers consider continent diversion to be the more attractive option.
- Many patients will avoid a cystectomy altogether because they have been told they will need an ileal conduit.



nighttime continence. So our older patients are doing the same as our younger patients in terms of leakage.

Dr. Sia Daneshmand:

So again, there's this notion that the older patients will not be as continent and that's just not true. This is hot off the press, we just presented this at one of our meetings and are sending it to our next meeting. This again don't worry so much about the graph but you could just see they look the same. This is long-term kidney function in patients who have slightly impaired kidney function already who are often not offered continent divergence CKD stands for chronic kidney disease. So in patients with chronic kidney disease, stage three, who underwent a neobladder with us, they seem to have the comparable long term renal function to those who had normal renal function. So we think that neobladder is a safe option in patients who have mildly impaired renal function as well and we have the data to prove it.

Day time continence

Age Grouping * Day Continence Crosstabulation

Count		Day Continence				Total
		Continent	1 pad	more than 1 pad	Incontinent	
Age Grouping	70 and younger	37	11	2	2	52
	older than 70	17	9	1	2	29
Total		54	20	3	4	81

Chi-squared analysis showed **no significant association between age and day time continence** ($\chi^2=1.53, p=0.675$)

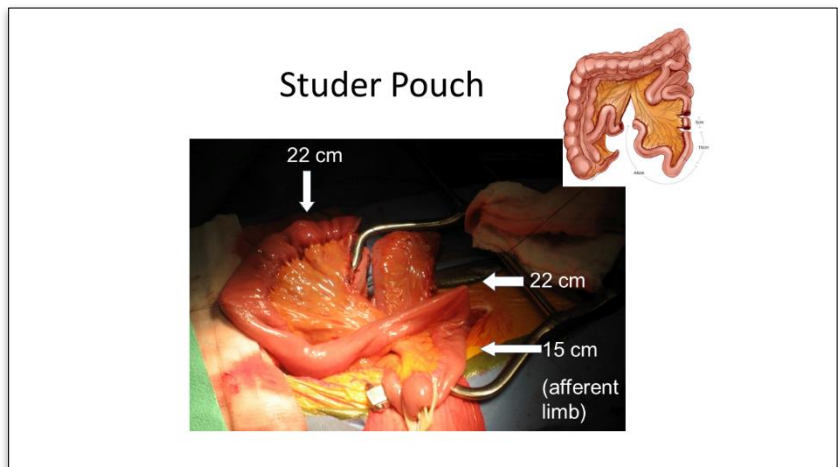
Night time continence

Age Grouping * Night Continence Crosstabulation

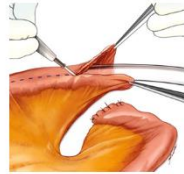
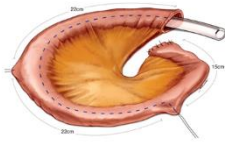
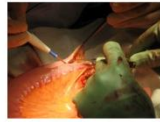
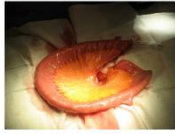
Count		Night Continence				Total
		Continent	1 pad	more than 1 pad	Incontinent	
Age Grouping	70 and younger	21	20	5	4	50
	older than 70	10	14	3	2	29
Total		31	34	8	6	79

Chi-squared analysis showed **no significant association between age and night time continence** ($\chi^2=.588, p=.899$)

The most common type is Studer and Folding pouch, you may have heard these names, but I'll just very briefly go through the Studer pouch. These are some surgical pictures if you're squeamish, you may not want to see this, but there's a schematic up there. We take a 40 overall a 60 centimeter segment of the intestine. We lay it out like this. Next. And then we open it just like that. We isolate it from the rest of the intestinal



Studer Pouch



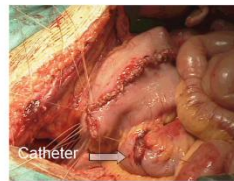
this thing expands, this thing will stretch. So here's the sutures that are connecting it down towards the urethra and there's a schematic of how that's done. The sutures are made connecting the neobladder to the urethra and the sphincter mechanism. The control mechanism is of course, on the urethra, not on the neobladder.

tract. We open it. And we fold, we sew the middle of it. And then we fold it in order to make a pouch out of this or something close to it.

Dr. Sia Daneshmand:

And then we connect it to the urethra. And we then connect, if you can see on the top right there, we connect the ureters. Those are the tubes from the kidneys. We connect it to this little limb or the chimney that leads to the neobladder, that's the reservoir. So that's how it's made. That's what it looks like in the operating room, just in case you wondered, and

Neobladder-urethral anastomosis



So what about selection? Let's talk a little bit about continence complications and reoperation rates. Next line. So here's the truth. We have one of the largest experience with neobladders. Between 2000 and 2014 we had 1,545 patients who had undergo a radical cystectomy. We've done over 2000 neobladders at USC. We gave questionnaires to all the patients. There were 153 male patients with 284 pad usage questionnaires that were collected. So some patients filled out more than one.

Prospective Evaluation of Continence Following Radical Cystectomy and Orthotopic Urinary Diversion Using a Validated Questionnaire

THE JOURNAL
of UROLOGY®

Thomas G. Clifford, Swar H. Shah, Soroush T. Bazargani, Gus Miranda, Jie Cai, Kevin Wayne, Hooman Djaladat, Anne K. Schuckman and Siamak Daneshmand*

- Forms collected from patients from Aug 2012 to Oct 2014
- Patients underwent RC between 2000 and 2014
 - **1545 patients**
- 153 male patients with available questionnaires
 - 284 pad usage questionnaires were collected
 - 243 interval distinct questionnaires were defined

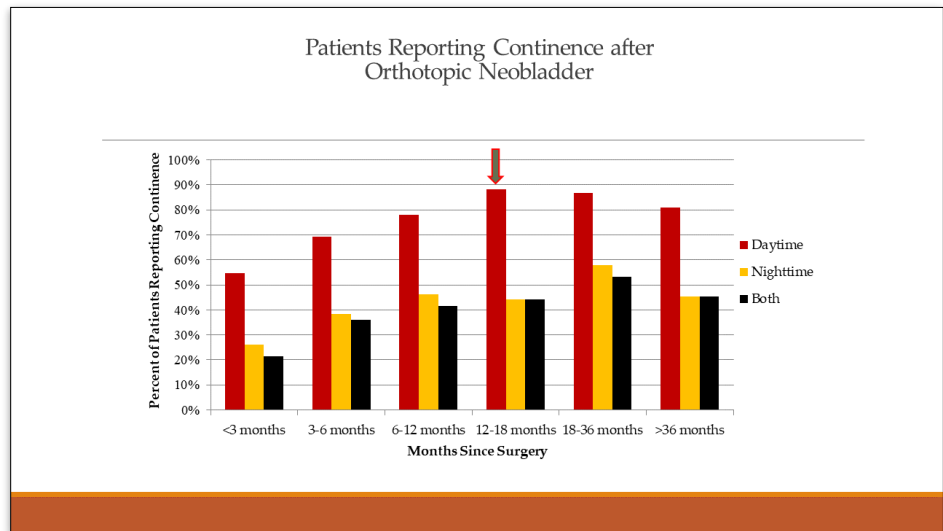
Dr. Sia Daneshmand:

And this is the questionnaire we gave them, looking at what kind of pad they use. This is very detailed. Is it wet? Is it slightly wet? Is it soaked? One to two pads? Three to four pads? How many pads are you wearing during the daytime and nighttime, and are you leaking mucus? So it was a detailed questionnaire that the patients filled out rather than us

documenting it in the chart. So this is the best way to collect data because these patients filled out.

And here's the graph, just look at the red bars there, and you can see at three months, three to six months and six to 12 months, and even 12 to 18, the red is daytime.

Continence is steadily increasing from 50% to close to 90% continence for the male patients. When you look at the yellow, the nighttime continence you can see it starts out at about 25 and it peaks close to about 50 or 60% of patients being dry at night. So these are the numbers. I tell patients, these are the real patient reported numbers and what we experience.



So overall, how about the catheterization rates? This is a big deal for patients. They really, they just had a TURBT the transurethral resection of the bladder tumor, and they don't want to have anything to do with catheterizations and someone is telling them they need to catheterize. Well, the overall catheterization rate in this cohort was only **13%**. Again, this is for males and the median time to catheterization, the average time to for patients to require catheterization was over a year. How about females? Let's briefly go through females. So we don't, there isn't as much data. Here's one of the articles we've published on female continence in this slide and I want to go through all of it, but basically the white is total control. Again, this is patient reported outcomes.

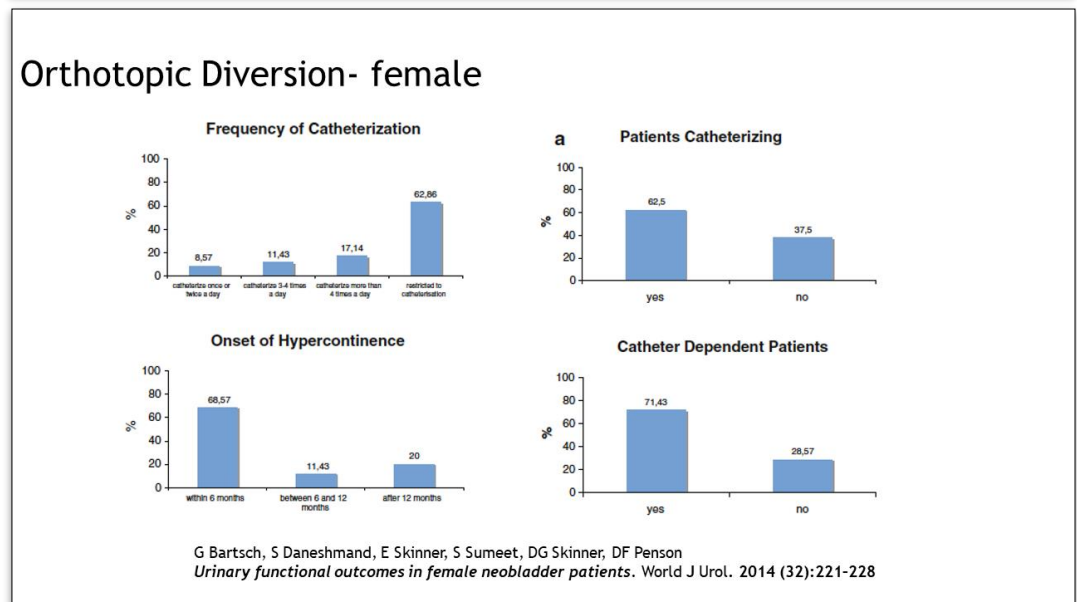
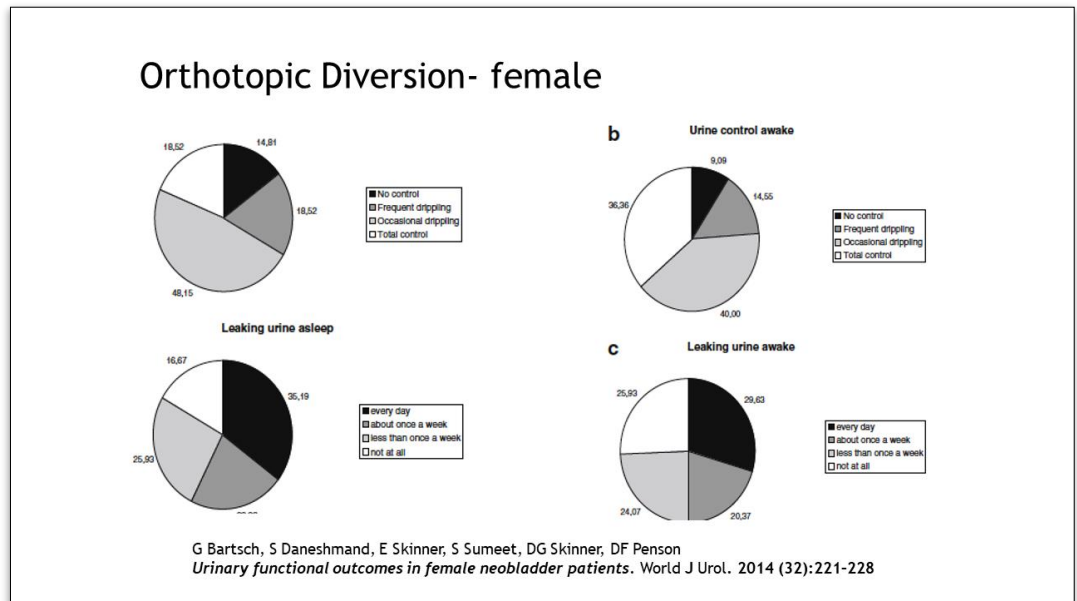
Dr. Sia Daneshmand:

Now this was a bit of a problem because we mailed the questionnaire and the patients who've mailed it back, that's the only data we have. So there's some bias here in who sends it back. But you can see

leaking urine while asleep. It's highly variable for women. Now you can see on the right side leaking while awake. So 30% of patients have total control. That's the whites. And then the dark is no control. Less than 10% of patients are reporting that they have no control at night. Next slide. This is frequency of catheterization. It's up to 60% of female patients require catheterization. But again, I think this is a cohort that ended up filling out those questionnaires and sending it to us.

So, in our more recent cohort, it's more like 30% of patients need to catheterize. I just want a highlight, there are other series many other centers that have reported on female continence rates. If you look to the right where it says

continence, you can see anywhere from 80 to 90% daytime continence and it's variable. We have one that's 30% and nighttime continence anywhere from 30 to 70%. Of course, the term continent in and of itself is variable in terms of what is the meaning of continent? Is it no pads or some pads? So looking at next slide, quality of life people ask us, which is better? Well, we can't tell you which is better. But these quality of life studies have been done.



Dr. Sia Daneshmand:

There's extensive literature actually on this, but there's very low scientific quality to this. It's very hard to compare. But the published evidence basically shows no difference in quality of life when comparing continent diversions and conduit, basically all the diversion option. So I tell the patient, look, pick what is comfortable for you. And that's the one that you're going to be happy with. You're not going to have regrets. And it's very hard to do a randomized type study to see which one's better. Some studies do show that neobladders have a better self image for the patients, but overall patients do quite well and are happy they're cured of their cancer. Next. The quality of life does decline after diagnosis and treatment of all cancers.

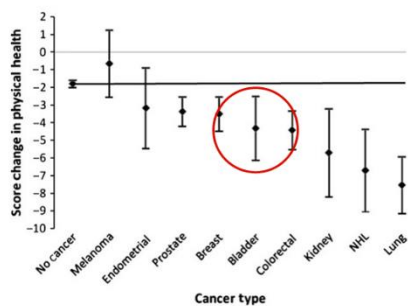
If you can see this, this is the decline in score of quality of life, and you can see bladder. So somewhere in the middle with kidney and lung cancer, there's even more declining quality of life . So I just wanted

Orthotopic Diversion in Females

AUTHOR	TYPE	NO. OF Pts	MEAN FOLLOW-UP (mo)	MEAN AGE (yr)	MORTALITY (%)	COMPLICATIONS [†]		CONTINENCE		IC (%)
						EARLY (%)	LATE (%)	DAY (%)	NIGHT (%)	
Stenot et al (2001)	Ileum	102	26	59	0	5	12	82	72	12
Granberg et al (2008)	Ileum (Studier)	59	29	62	0	22	5	90	57	35
Al-Eid et al (2008)	Ileum, serous-lined extramural tunnel	192	51	54	2	16	35	92	72	16
Stein et al (2009)	Ileum (Studier or T-pouch)	120 (n = 56 for continence results)	103	66	2.5	32	26	77 [†]	66 [†]	61 [†] (39% dependent on IC to void)
Jentzmik et al (2012)	Ileum (Hautman)	131	56	61	1.7	16	NA	82.4 [†]	75.9 [†]	58 [†]
Anderson et al (2012)	NA	49	37	60	NA	NA	NA	57	45	31
Bartsch et al (2014)	Ileum (Studier or T-pouch)	56	63	64	NA	NA	NA	30	35	62 (45% dependent on IC to void)

*Complications reported related to urinary diversion, definitions vary by report.
[†]Continence results from validated patient-completed questionnaires.
 IC, intermittent catheterization to empty neobladder; NA, not available from report.

QOL Declines After Diagnosis/Treatment

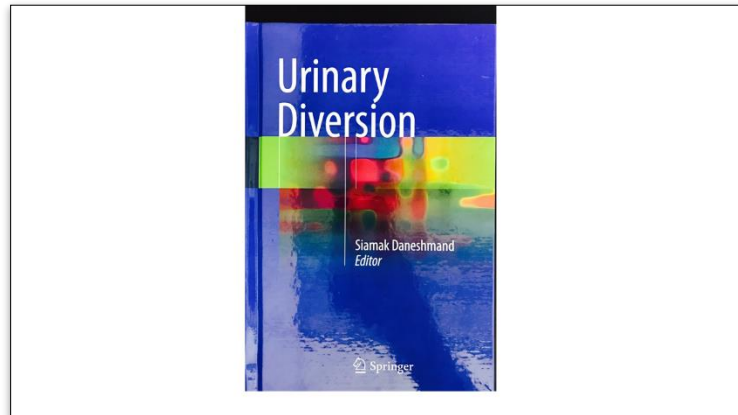


Reeve et al. J Natl Cancer Inst 2009;101:860-68.

to show it in perspective with the other cancers. It does come back a little bit close to baseline, but not same as baseline. A lot's been written about this, I write about this topic a lot. This is an area that's near and dear to my heart. There are a lot of controversies choosing the rights diversion. I put this in quotes because there is no right diversion. You have to weigh the risks and benefits based on the lifestyle and motivation of priorities.

Dr. Sia Daneshmand:

And so I think our job is to provide patients with realistic expectations, informing them of the continence and the complication rates at your particular center. Next slide. And that's it for me. I have a book on urinary diversion. It's got 15 chapters on the various aspects written by authorities in the field. And it's mostly technical, but this is available on whatever book store you choose.



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The slide contains a collection of logos for various pharmaceutical and biotech companies. At the top, it says "BCAN would like to thank our Patient Insight Webinar sponsors". Below this, there is a grid of logos: Astellas (red star), Seattle Genetics (green leaf), Bristol Myers Squibb (black and white), EMD Serono (blue and white), Pfizer (blue oval), FerGene (red and white), Janssen Oncology (blue and white), Genentech (blue and white, with "A Member of the Roche Group" below), Merck (green and white, with "INVENTING FOR LIFE" below), Photocure (red circle), and The Bladder Cancer Company (black and white). At the bottom right is the BCAN logo, which features a stylized sun icon above the text "BCAN" and "Bladder Cancer Advocacy Network" below it.