A MRI/US Fusion treatment for localized Prostate Cancer that preserves sexual ejaculatory and improves urinary function while destroying cancerous tumor

Focalyx\textsuperscript{Tx}\textsubscript{Cryo}
FOCALYX TxCryo - Fusion Targeted Cryoablation of the Prostate

Naturally, receiving a Prostate Cancer diagnosis evokes tremendous worries in you and your loving ones. However, given the recent advances in modern medicine, the fact is that most men will beat prostate cancer.

Indeed, several studies have shown that for many men the odds of experiencing a side effect from a whole prostate treatments - given to remove or eradicate prostate cancer - may be far greater than the risk impose on death by this disease.

Thus our paradigm is a holistic approach that emphasizes quality of life. The premise is to destroy the tissue with cancer while preserving tissue without disease and therefore, prostate and adjacent organs function is preserved.

We believe that patients must have all the information available for thorough decision making. Ask our physicians for the pros and cons of each approach and specifically ask your self and your doctor the question: why this approach fits me best ? what are the risks? and most importantly what are my options if the cancer recurs or comes back?

Management of Prostate Cancer aimed to preserve and improve quality of life for those suffering from this disease

Fusion Targeted Cryoablation represents a novel technique that combines the precision of MRI findings with the practicality of ultrasound imaging. The fusion of both of this images yields a GPS of the prostate where we can direct treatment with fine needles at -40o f temperatures that destroy the targeted area that contains the cancer.
What is Cryotherapy?

Cryotherapy is a FDA approved treatment modality for the management of Prostate Cancer.

Cryotherapy involves freezing the cancer cells and cutting off their blood supply. Tiny needles are placed right into the tumor. Argon gases are passed through the needles and exchanged with helium gases. This causes a freezing and warming cycle. The frozen, dead tissue then thaws and is naturally absorbed by the body.

Like any other treatment for prostate cancer - the surgical technique for cryoablation of the prostate has evolved.

In the early days of prostate cryoablation, decades back, it employed probes that used liquid nitrogen and monitoring was accomplished thru a digital rectal exam. The introduction of transrectal ultrasound probes in the 1980 proved instrumental for real-time monitoring using sonography. The iceball and its edges were visible this way adding a safety layer for the patient. However, controlling the iceball and flow of liquid nitrogen proved difficult. Gas driven cryoablation using argon(freezing) and Helium (thawing) changed the profile of this treatment option.

This millennium has witnessed two significant improvements. First the improvement in the cryotherapy machines where currently, each cryoprobe can be controlled individually and second the emerge of Focalyx.

What is FocalyxTxCryo

FocalyxTx Cryotherapy represents a complete disruption from conventional Prostate Cryoablation.

FocalyxTxCryo dwells on a quality of life paradigm: preservation of sexual and ejaculatory function, improvement in Urinary function and precise MRI/US fusion cancer kill.

The concept of a prostate GPS has been taken to another level by Focalyx. Thus the MRI findings outline projected on the ultrasound image brings a 3D perspective that allows target driven precision of the cancer tissue. Thus prostate cancer multi-focality is addressed. In addition, further safety is ensured by precise determination of the urethra, seminal vesicles and prostate boundaries.
Will FocalyxTxCryo kill my Prostate Cancer?

Without question the targeted tissue will be destroyed.

Eligibility is a critical issue, however, most men diagnosed with Prostate Cancer at early stages are eligible. Most men are diagnosed with what called low risk prostate cancer (PSA under 10, Gleason 6 or Grade 1 Cancers that are either non-palpable or palpable but involving less than 50% of 1 lobe) or low volume intermediate risk prostate cancer (PSA between 10 and 20 ng/ml or tumor palpable >50% of 1 lobe or Gleason 7 or Grade 2 or 3) these patients are fine candidates for FocalyxTxCryo. Furthermore, older men with good quality of life and low volume high risk prostate cancers are candidates as well. However, you must have a thorough discussion with your Urologist

The efficacy in cancer control is measured by years from progression and survival. The graph below shows the freedom from progression rates associated to prostate cryablation

**Percentage(%) of patients with freedom from PSA progression after Prostate cancer treatment.** The number indicates the % of men who remained disease free at the time of follow up*

*The graph shows freedom from PSA progression as published in several medical journals. The period of follow up for most modalities including cryotherapy is at least 10 years. However for PRR and HIFU the follow up interval is shorter*
Who is eligible for targeted fusion cryotherapy - FocalyxTx Cryo?

Your Urologist will discuss with you all treatment options for the management of your prostate cancer. Several variables will be incorporated in the decision making process, among them: Clinical stage (how extensive is your cancer), Gleason Score (how aggressive is it), PSA level, your Age, your life expectation, your urinary and sexual function. Currently the vast majority ~80% are eligible. In addition, FocalyxTxCryo is an outstanding option to salvage men who have been treated and failed radiation therapy.

Unlike traditional Cryotherapy procedures, surgery or radiation therapy, Focalyx Prostate Cryoablation - FocalyxTxCryo - aims at a targeted region(s) of the prostate gland that harbors cancer tissue. It's a minimally invasive procedure that can be performed either in an ambulatory center or the office center under local anesthesia.
What are the benefits of Targeted Fusion Prostate Cryoablation - FocalyxTxCryo?

There are several advantages, among them:

- **A minimally invasive - office based** (without incisions) precise curative approach
- **Source of energy is freezing (Cryoablation) has over 10 years of clinical data**\(^1\) that supports this energy source security and efficacy destroying tissue, particularly cancer tissue
- **Individual tailored treatment** executed in an ambulatory or office center
- **Avoids hospital stay** and risk hospital acquired infections
- **Expedited recovery time** fast return to regular daily activities
- **Minimal risk of rectal irritation**\(^2\)
- **Improvement in Urinary Function.** Unlike most prostate cancer treatments that have strong associations with voiding dysfunction and urinary incontinence. Targeted fusion cryoablation provides opportunity for concomitant destruction of prostate enlargement tissue leading to improved flow rates and efficient voiding.\(^3,4\)
- **No postoperative pain**
- **Outstanding choice in rescuing patients whom experience recurrence after management with other approaches such as** radiotherapy or seeds
- **It does not burn any bridges.** Patients are carefully monitored and those who prove to harbor more aggressive cancers can be managed with robotic surgery or external beam radiation.

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\(^1\)Cohen et al. Urology (2008)

\(^2\)Langenhuijsen et al. European Urology (2009)

\(^3\)Kimura et al. Urology (2010)

What are the risks and possible secondary side effects?

FocalyxTx Cryotherapy does not escape the old adage of any action generates reaction. However, the precision involved in the treatment delivery ensures a very low probability of any significant side effect. Prostate intervention may trigger Urinary tract infections, however the risk is under 1% because of the transperineal approach. The most common adverse event is urinary retention after removal of the Foley catheter. This is why we take our time to ensure prostate swelling is greatly diminished at the time of pulling the catheter out. Transient urinary incontinence may happen albeit is rare. Sexual dysfunction may occur, specially if there is preexisting weakness of erections. Otherwise if happens should be transient and limited to weeks time.

How long is the procedure?

The average procedure time is under 60 minutes, However, there set up time and also recovery time so expect at least 90 minutes. Importantly, the procedure is ambulatory, so you will go home the same day. Have a relative or friend to help transport you home as no driving is allowed after the procedure.
How would I feel after the procedure?

You will experience some discomfort after the procedure, specially if a indwelling foley is left in (happens 50% of time). All the discomfort subsides with oral medication. You may also see some skin discoloration or hematoma in the perineal area. This will improve and subside within days and is related to the swelling of the prostate secondary to the ice ball.

How long before I can resume normal activities?

Your Focalyx physician will provide details based on the specifics of your treatment. In general, if no catheter was needed you may return to work within days. We recomend for you to take it easy for a week or so. You will be active but remember your body will be on healing mode.

What happen with other activities such as sports?

Your physician will provide recommendations, but in general full-activity can take place within 2 weeks of your FocalyxTx Cryotherapy treatment.

“I feel great, my strength is back and I feel invigorated.”
Can or will FocalyxTxCryo affect my Sexual Health?

**A crucial question and the bottom line: not likely.** However it's critical to elaborate on the elements that confound when evaluating sexual health and expectations after any management option for prostate cancer.

Some men who are observed after a diagnosis of prostate cancer will develop erectile dysfunction (ED). In reality most men will. This is because over time, with aging the incidence of ED or impotency goes up. Population studies have clearly shown that the prevalence of ED rises from ~30% in the 40s and 50s decade of life to about 75% for men over 70 years of age. ED is commonly related to other illnesses like diabetes, high blood pressure or heart disease or those with elevated cholesterol. These are frequent among men with prostate cancer. Thus, importantly, to set expectations right, the quality of erection at the time of diagnosis must be established with precision.

ED is a common side effect of traditional management with surgery or radiation. In the case of surgery, neurotrauma from nerve dissection, or nerves excision are a likely source. As for radiation, damage may be from direct radiation effects or from neo-vascular effects that happens later over time.

FocalyxTxCryo is different as its planned cancer kill is done by MRI imaging and has 2 safety areas: 1-The surrounding treatment margin and 2- The 3D prostate visualization. Both allow the urological surgeon to know the boundaries of treatment and how close may be getting from the nerve bundles. Importantly, some tumors may be close to a nerve bundle and it may have to be taken out, just like the cancer, but the contra-lateral one is preserved. *In addition, the lowest temperature reached at the bundles area can be measured.*

Because FocalyxTxCryo targets directly cancer tissue and preserves prostate function, the **majority of patients see no ED after treatment.** Furthermore, *ejaculation is preserved among the vast majority of patients.*
How is urinary function affected?

Bottom line: **expect improvement** in flow rates and decrease in urinary symptoms

Urinary function is at heart for men treated for prostate cancer. This is because of concomitant prostate enlargement, consequential bladder hypoertension and over-activity, disruption to external urethral sphincter or a combination of all. Indeed, commonly men with prostate cancer experiment urgency, frequency, nocturia, weakness and intermitency in urinary flow. Fortunately, those symptoms are not due to prostate cancer - unless is a very advanced stage - but rather due to obstruction from concomitant prostate enlargement.

Radical surgery does remove the obstructive components of enlargement, but changes voiding forever. Sure the flow improves significantly, but stopping it or controlling it may be a challenge and about 15% of men will require a pad for involuntary loss of urine. Its always critical to ask your Urologist of what are his patients continence rates after radical prostatectomy. Irradiated patients face hazards that may lead to permanent bladder overactivity and perennial urgency and intermitency. It happens to about 1 out 8 irradiated men. Unfortunately 1 in 10 may develop something more pervasive: radiation cystitis.

There is basically no risk of urinary incontinence associated to FocalyxTxCryo. In fact, our internal data analysis of over 250 men treated with FocalyxTxCryo over a 3 year period showed significant objective improvement in urinary flow rates from an average of 6 ml per second to 11 ml/sec. Maximal flow rates improved by 88% and the amount of residual urine in the bladder decreased by 60%.

Roughly 50% of FocalyxTxCryo patients may go home with an indwelling Foley catheter, which is removed 5-7 days later. About 1 of 10 may require a catheter for a period longer than a week. This is by far the most common adverse event yet carries no comparison to those that are associated with surgery or radiation.

Good urinary continence is a fundamental fact associated with Prostate Cryotherapy in general and a significant reason why is the preferred salvage modality for men who experience prostate cancer recurrence after radiation therapy.
What should be my long term expectations?

The bottom line: a greater than 70% chance of having a negative prostate biopsy and year after the procedure.

However, it's very important to understand that MRI/US fusion target cryotherapy (FocalyxTxCryo) accomplish targeted tissue destruction. Therefore, if the same conditions that lead to initial cancer development remain, it's quite possible that a new cancer could form from the reminder of prostatic tissue, that often harbors atrophy, inflammation but could also have also atypical acinar proliferation or high grade intraepithelial neoplasia. The latter two are considered pre-malignant lesions of the prostate. You will sample the treated area evaluating the area not only by imaging but also pathologically.

The other critical factor to consider relates on how the diagnosis of prostate cancer was made. If the diagnosis was obtained by a random prostate biopsy or a cognitive MRI guided approach, it's possible that existing cancer was missed.

The Focalyx follow up protocol is compulsive on the need of a FocalyxBx a year after FocalyxTxCryo.

This biopsy is performed using real-time MRI/US fusion and while it's possible to miss cancer, it's though unlikely. Specially any significant cancer. Moreover, that follow up biopsy will sample the treated area evaluating the area not only by imaging but also pathologically. Our internal analysis of over 250 patients shows an under 5% probability of prostate cancer detection 1-year after FocalyxTxCryo.

Importantly, in those men who prostate cancer is identified, it usually of smaller volume and over 90% rather receive a FocalyxTxCryo for such tumors.
FocalyxTxCryo as a Salvage option

Data from the Cancer of the Prostate Strategic Urologic Research Endeavor (CapSURE) suggest that over 50% of men managed with external beam radiation may experiment cancer recurrence. These so-called Radiation Failures are often managed with primary hormonal (androgen) deprivation. The latter effectively controls androgen sensitive cells, however many patients experience lifetime side effects, among them chronic fatigue and hot flashes.

The initial suspicion of recurrence is commonly signaled by post radiation PSA elevation. A FocalyxBx procedure is recommended for this patients. Importantly, time is of essence. Successful Salvage Prostate Cryoablation is associated to:

* PSA levels < 10 ng/ml at time of Salvage therapy
* Clinical T1 or T2 disease
* MRI verified tumor confined

Unlike traditional salvage cryoablation, FocalyxTxCryo focused on the proven areas of recurrence. A negative metastatic workup is reassuring and may prevent concomitant use of androgen deprivation therapy (ADT). This is critical to preserve quality of life. ADT slows down tumor progression in a significant way, However, side effects albeit tolerable are a frequent annoyance. Furthermore, the FDA issued an advisory warning recently highlighting the association between ADT and cardiovascular diseases.

Ask your urologist about your eligibility for Salvage Cryoablation using a FocalyxTxCryo protocol.

Salvage Radical Prostatectomy represents another option for radio-recurrent prostate cancer patients. However, it carried significant side effects in terms of ED and Urinary Incontinence and the potential to more severe adverse events such as fistula formation. Furthermore, it is truly of benefit in a small number of patients and patient selection is crucial.
What are the advantages of FocalyxTxCryo?

• Potential curative therapy
• Performed in a single session in ambulatory or office setting
• Minimal risk of incontinence
• No risk for urethral strictures
• No surgical incision required
• Potential avoidance of ADT
• Expedited recovery
• If needed, it could be repeated

What are the disadvantages of Androgen Deprivation therapy - ADT?

• Slows down prostate cancer by halting replication of androgens sensitive cells
• Side effects:
  o Decrease in mineral bone density, associated with fractures
  o Hinders cardiac function
  o Alters glucose regulation, making diabetes more likely
  o Changes in fat distribution, Gynecomastia
  o Chronic Fatigue
  o Hot flashes
  o Lack of sexual interest
  o Cognitive impairment

Discuss with your urologist of whether you are a good candidate for a FocalyxTxCryo.
Be alert if you experience post radiation PSA elevation

Risk factors that predict a favorable Prostate Cryoablation response:

• PSA levels under 10 ng/ml
• Tumor that is not palpable
• Tumor that is palpable but within the boundaries of the prostate on the MRI