Vessel-sparing radiation and functional anatomy-based preservation for erectile function after prostate radiotherapy

Jae Y Lee, Daniel E Spratt*, Adam L Liss, Patrick W McLaughlin*

Lancet Oncol 2016; 17: e198–208

*Authors contributed equally

Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, USA (J Y Lee MD, D E Spratt MD, A L Liss MD, Prof P W McLaughlin MD); **Agnesian Cancer Center, Fond du Lac, WI, USA** (A L Liss); **and Assarian Cancer Center, Novi, MI, USA** (Prof P W McLaughlin)

Correspondence to:
Prof Patrick W McLaughlin, University of Michigan, Assarian Cancer Center, Department of Radiation Oncology, Novi, MI 48374, USA
mclaughb@med.umich.edu

Treatment selection for men undergoing curative treatment for prostate cancer is often a challenging decision in view of the goal of maximising cure while maintaining quality of life. Previous quality-of-life comparisons suggest that specific outcomes are associated with type of treatment (surgery *vs* radiation); however, the functional anatomy approach, starting with nerve-sparing prostatectomy, assumes that quality-of-life outcomes are established by anatomic preservation. Emerging applications of the functional anatomy approach for prostate radiation will ultimately allow for individualised treatments that address the normal tissue variants visible on MRI. Such approaches will encompass all essential functions affected by treatment including genitourinary, rectal, and sexual functions. In this Review, we outline the current techniques in functional anatomy-based preservation related to sexual outcomes, and outline the capacity of vessel-sparing radiotherapy to preserve sexual function in 90% of patients at the 5 year follow-up while maintaining excellent cure rates.

Introduction

Cure and quality of life is the modern definition of successful treatment for prostate cancer. Prostate-specific antigen screening has improved the chance of prostate cancer detection at a highly curable timepoint in the progression of the disease. Treatment decisions are now influenced by the probable effect of the treatment on genitourinary, gastrointestinal, and sexual functions. Preservation of sexual function is often a decisive concern for men diagnosed in the modern era because sexual function relates closely with treatment outcome satisfaction.[1,2] Active surveillance of patients with prostate cancer is the most effective strategy to preserve sexual function;[3,4] however, only 76% of patients remain untreated and on surveillance at 5 years, and this rate decreases further to 55% at 15 years.[5]

Surgical strategies to preserve sexual function in men with prostate cancer have evolved from traditional nerve-sparing radical prostatectomies to modern robotic approaches that address the wide variation in nerve anatomy by also sparing the lateral prostatic fascia (Veil of Aphrodite).[6,7] Hormonal treatment strategies to restrict the profound sexual and non-sexual effects of total androgen blockade include attempts to omit androgen deprivation in high-risk patients with surgery or combination brachytherapy and external beam radiotherapy.[8,9] Strategies to preserve sexual function have developed in radiation oncology from sparing the penile bulb to MRI-planned approaches that accurately define the prostate and critical vascular erectile tissues.

Attempts to improve sexual function outcomes after definitive treatment for prostate cancer have been limited by several barriers. The present cure and quality-of-life era began with the development of instruments to objectively assess and compare the effect of different treatments on essential functions.[10,11] Although symptom scores can be valuable when attempting to define the mechanism of sexual dysfunction, quality of life is better identified by measuring the extent of bother associated with sexual dysfunction symptoms. One limitation of measuring the extent of bother is the fact that, with time, the bother from a specific change, such as profound erectile dysfunction, might lessen as the individual adapts and accepts this change. At present, no single assessment instrument measures the full range of post-treatment symptoms objectively. This range of dysfunction is broad and includes men with a full loss of libido but no sexual frustration, to men with strong libido and an inability to sustain an erection, to men with an intact libido, erections, climax but anger at the loss of ejaculate. Beyond physical changes, the psychological costs associated with prostate cancer treatment include performance anxiety causing sexual avoidance, changed relationships with potential sexual partners, weakened sexual fantasy, and a diminished sense of masculinity.[12] This complex range of dysfunction obscures simplistic causative correlations between anatomy and erectile dysfunction.

Additionally, sexual function is well known to change with age. Between age 65 years and 75 years, most men will lose sexual function even without prostate cancer treatment.[13,14] Furthermore, the increasing incidence of chronic diseases with old age, including depression, can also produce changes that diminish sexual function.[15] These changes can be gradual and often occur in parallel to changes that are noted in women, leading some couples to adopt strategies for intimacy beyond traditional intercourse. Therefore, for some men, validating erectile function by performance in sexual intercourse alone reaches an obvious limitation.

Another limitation of the vast majority of previous radiation oncology studies is CT imaging. The use of MRI is increasing in the detection and prebiopsy assessment of prostate cancer, as well as in establishing which patients are best for active surveillance.[16] MRI has also radically changed the planning of prostate radiotherapy by improving the delineation of the prostate. With appropriate training, interobserver variation in prostate and normal tissue definition on the same patient

has narrowed.[17,18] MRI-based planning has shown that the prostate was often overestimated with CT-based planning resulting in inclusion of critical adjacent structures affecting quality of life after treatment. Of note, every millimetre of overestimation affects the radiation dose to the urinary sphincter, rectal, or sexual structures. Additionally, MRI has disclosed variations in the essential adjacent anatomy relevant to sexual function—in other words, a one size fits all approach does not work. One striking example in a study examining the distributive pattern of nerves surrounding the prostate, is the fact that only 49 (52%) of 95 men have a clearly defined nerve bundle in the classic posterior lateral position.[19] This fact challenges all previous nerve bundle correlation studies that assumed a classic posterolateral nerve bundle configuration.[20–23] To this end, MRI-based radiation planning represents a full departure from CT-based target and essential adjacent anatomy definition. MRI will ultimately allow correlation of dysfunction with variant anatomy.

Despite confounding complexities of functional change, rapidly evolving sexual practice, and anatomical variation, reason exists to be hopeful that a thorough, functional anatomy-based approach will ultimately allow patient expectation to be replaced with an actual prediction of outcomes. Similar models based on medical comorbidities have been constructed to predict erectile function after treatment for prostate cancer, although these models do not take into account anatomical considerations.[24] In the ideal situation, a specific patient with known comorbidities, baseline function, and well defined tumour and essential adjacent anatomy, will ultimately know before choosing treatment, what their probable sexual function and tumour control outcome will be (figure 1).

In this Review, we discuss functional anatomy-based preservation and vessel-sparing radiotherapy to preserve sexual function in men with prostate cancer, with the hope that patients can choose the optimum balance of cure and quality of life when deciding treatment.

Functional anatomy-based preservation

In addition to a properly functioning neuroendocrine axis, erectile function is mediated through several nerve and vascular pathways within the pelvis. Required elements include an intact neural pathway that supplies nitric oxide and terminates at erectile tissue, an arterial supply of blood to provide engorgement of the corporal sinusoids, and adequate distention of erectile tissue to restrict venous outflow for maintenance of penile rigidity.[25,26] Classically, neurovascular bundles course over the lateral rectal surface and continue posteriorly and laterally adjacent to the seminal vesicle and superior prostate.[27] The nerves continue inferiorly along the external sphincter and terminate at the erectile tissue. Vascular elements include the internal pudendal arteries, which provide afferent blood supply and generally do not come in contact with the prostate. The dorsal venous complex runs over the anterior prostate and provides venous drainage for the penis.

Evidence has shown that vascular elements have a crucial role in postradiation erectile dysfunction.

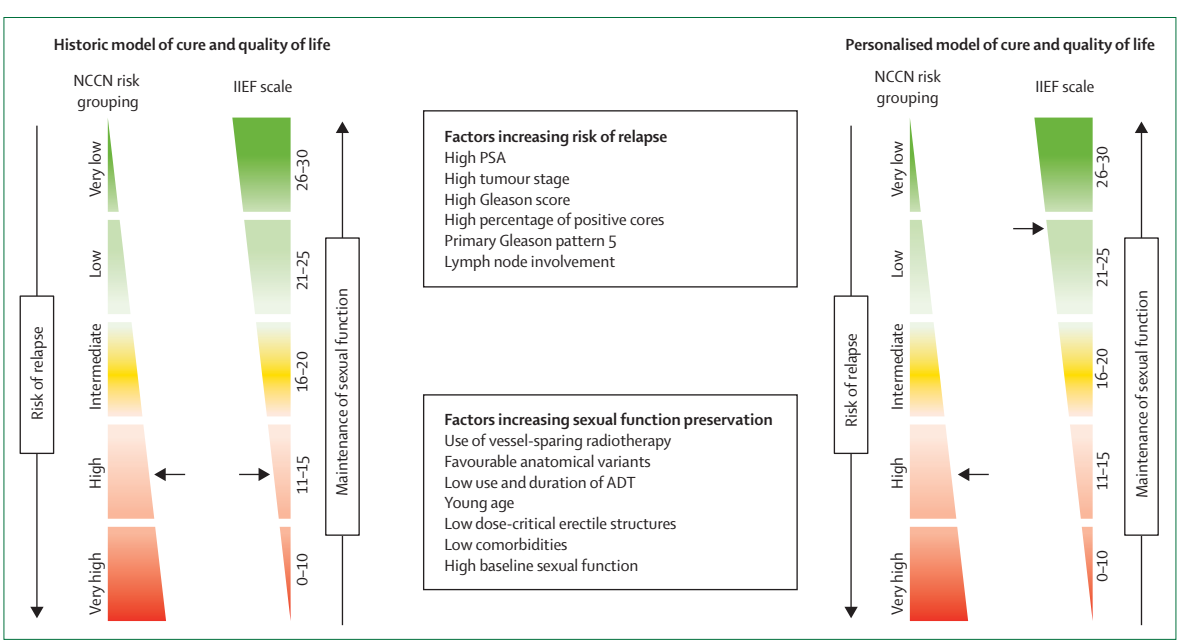

Figure 1: **Balance of cure and quality of life**
Risk of relapse and maintenance of sexual function can be disconnected by personalising treatment in the modern model (right) versus the connected historic model (left). ADT=androgen deprivation treatment. IIEF=International Index of Erectile Function. NCCN=National Comprehensive Cancer Network. PSA=prostate specific antigen.