Perineural Spread of Prostate Cancer

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Goals and Objectives

• Describe the innervation and relevant neuroanatomy of the prostate gland and lumbosacral plexus.

• Review the imaging features and patterns of perineural tumor spread of prostate carcinoma.

• Identify potential pitfalls and mimickers which could lead to misdiagnosis of perineural tumor spread.

Target Audience

• Radiologists and trainees who interpret pelvic and prostate MRI, and FDG and Choline PET CT/MRI.
Background

• Spread of tumor along nerves, known as perineural spread (PNS), is a well known phenomenon in head and neck malignancies.

• Perineural invasion (PNI) in prostate cancer is present in 7-43% of all prostate biopsies\(^1\). In the setting of PNI, extension along nerves is a logical method of metastatic spread of tumor.

• However, PNS of prostate cancer is a poorly described, yet increasingly recognized phenomenon in pelvic malignancies, including prostate carcinoma\(^2,3,4\).
Prostate Neuroanatomy

• Innervation of the prostate is supplied by the inferior hypogastric (pelvic) plexus

• Inferior Hypogastric/Pelvis plexus
  • Mixed sympathetic and parasympathetic innervation
  • Derived from S2-S4 pelvic splanchnic nerves
    • Also gets contributions from superior hypogastric plexus
  • Extends to other pelvic organs
    • Rectal plexus, Vesicoureteric plexus, uterovaginal plexus/prostatic plexus
  • Located beside the rectum approximately 7cm from anal verge \(^5,6\)

The pelvic plexus.
The Surgical Anatomy of the Prostate
Reeves, Fairleigh, MB, BS, Prostate Cancer, Chapter 29, 253-263
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Sympathetic and parasympathetic contributions to the pelvic autonomic nervous plexus.

Surgical, Radiographic, and Endoscopic Anatomy of the Male Pelvis
Chung, Benjamin I., MD, Campbell-Walsh Urology, 68, 1611-1630.e1
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Innervation of the lower urinary tract and male genitalia. (Redrawn with permission from Dyck P, Thomas PK, 2005, Peripheral Neuropathy, Saunders, Elsevier.) Bladder, prostate and urethra
Standing, Susan, MBE, PhD, DSc, FKC, Hon FAS, Hon FRCS, Gray's Anatomy, Chapter 75, 1255-1271.e1
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Lumbosacral plexus anatomy

- Ventral rami of L1-L4 spinal nerves contribute to the lumbar plexus just posterior to psoas muscle\(^7\).

- Lumbar plexus communicates with sacral plexus via the lumbosacral trunk/cord.

- Ventral rami of L4-S3 nerve roots converge just anterior to piriformis to form sacral plexus\(^8\).
Perineural Invasion (PNI) and Spread

• Diagnosis of PNI\textsuperscript{9}
  • Tumor cells in any of the 3 layers of the nerve sheath.
  • Tumor foci outside of the nerve with involvement of ≥33% of the nerve's circumference are sufficient features for calling PNI\textsuperscript{9}.

• Literature is controversial regarding the prognostic significance of PNI at biopsy\textsuperscript{10}, though some suggest that disease free survival, cancer specific survival, and overall survival are worse in those with PNI\textsuperscript{11}.

• Traditional theories suggested PNS occurred due to tumor spreading along the “path of least resistance.”

• New evidence suggests signaling between tumors cells and nerves plays a key role in driving PNS.
Imaging Findings of PNS

- Nerve thickening/enlargement
- Widening of neural foramen
- Loss of fat surrounding nerve
- Abnormal T2 signal
- Contrast enhancement
- Increased radiotracer activity on PET CT/MRI$^{12}$

Axial T1W

Axial T2WFS

Axial post gad SPGR
Perineural tumor spread

65-year-old male with biopsy-proven perineural spread of prostate cancer.

**Enlargement** and **gadolinium enhancement** of the left sciatic nerve (A) and left S2 and S3 nerves (B).

**Increased FDG uptake** along the left sacral nerves (C, D).
63-year-old male with history of prostate cancer status post remote prostatectomy with biochemical recurrence.

**Enhancing soft tissue** infiltrating along the left mesorectal fascia (A) and proximal left sciatic nerve B).

Abnormal **choline uptake** in the same distribution (C, D).
77 yo M history of prostate CA with prostatectomy presenting with right lumbosacral plexopathy in the setting of biochemical recurrence of prostate carcinoma.

Nerve thickening, **increased T2 signal** (A, D) **contrast enhancement** (B, E) and **increased C-11 choline activity** on PET/CT (C, F) along the right S1 nerve extending along the right sciatic nerve.
Perineural tumor spread

A - axial post gad SPGR

B - axial fused FDG PET/MRI

C - axial T2WFS

D - axial fused FDG PET/MRI

E - axial T2WFS

F - axial fused FDG PET/MRI

G - coronal postgad T1WFS

H - coronal fused FDG-PET/MRI

65 year old with history of prostatectomy presenting with right lumbosacral plexopathy in the setting of biochemical recurrence.

Thickening, enhancement (A, G), and increased T2 signal (C) along the right S2 and S3 nerves extending along the sciatic nerve (E). Associated increased FDG uptake in the same distribution (B, D, F, H).
78 year old status post prostatectomy with biochemical recurrence of prostate carcinoma.

**Thickening** of the right **mesorectal fascia** (A) with associated **contrast enhancement** (D) and **C11-choline uptake** (B). Additional enhancement (C, F) and C11-choline uptake (E, G) along the right S3 nerve root.
Perineural tumor spread

86 year old with hormone refractory metastatic prostate carcinoma.

Soft tissue thickening and increased C11-choline uptake within the right mesorectal fascia (A, C) extending posteriorly to involve the right sciatic nerve (B, D) and right S3 nerve (E).
Perineural tumor spread

79 year old with biochemical recurrence of prostate cancer after prostatectomy.

Increased choline uptake along the left S1 (B, C) and S2 nerves (A, D), extending to the sacral plexus (D), sciatic nerve (D, E), and in the left mesorectal fascia (E).
Potential Pitfalls and mimickers

- Peripheral nerve sheath tumors
- Inflammatory or Demyelinating Conditions
  - Guillain-Barré syndrome
  - Charcot-Marie-Tooth Disease
- Systemic Diseases
  - Amyloidosis
  - Ischemic lumbrosacral plexus neuropathy
  - Diabetic plexopathy
- Radiation neuropathy\textsuperscript{12}
Demyelination

69 year old male with history of prostate cancer status post prostatectomy presenting with right lower extremity weakness.

**Thickening and increased T2 signal** (A) of the proximal right sciatic nerve, with associated **contrast enhancement** (B).

**No abnormal FDG uptake in right sciatic nerve** (C).

Biopsy and EMG consistent with chronic inflammatory demyelinating polyradiculopathy.
Demyelination

79 year old with history of prostate cancer status post prostatectomy presenting with new onset right lumbosacral plexopathy.

Thickening, **increased T2 signal** (A), and **enhancement** (B) of the lumbosacral plexus and L5 nerves. No associated increased C11-choline uptake (C).

Biopsy demonstrated segmental demyelination and inflammation with no evidence of malignant cells.
78 year old with history of pelvic radiation for prostate cancer presenting with left lumbosacral plexopathy. Marked thickening, increased T2 signal (A), enhancement (D) and increased FDG (B, E) and choline (C, F) uptake along the S1, S2 nerves extending to the sciatic nerve (A, C). Biopsy showed malignant peripheral nerve sheath tumor.
Conclusions

• Although poorly understood, perineural spread of prostate carcinoma is an increasingly recognized phenomenon.

• With advances in modern prostate imaging, including increased usage of PET/MRI, we suspect perineural spread will be an increasingly common finding.

• Close attention should be given to the lumbosacral plexus on prostate imaging, especially in the setting of biochemical recurrence of prostate CA with or without plexopathy symptoms.
References


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