Novel Scan Pinpoints Malignant Lymph Nodes in Prostate Cancer

BY JEFF EVANS
Senior Writer

ORLANDO — New modalities for detecting prostate cancer metastases may help physicians target treatment more effectively to diseased tissues, speakers said at a symposium on prostate cancer sponsored by the American Society of Clinical Oncology.

Current staging of the lymph nodes of patients with intermediate- or high-risk prostate cancer involves noninvasive tests such as CT and MRI, or the gold standard procedure of pelvic lymphadenectomy, noted Mukesh Harisinghani, M.D., of Massachusetts General Hospital, Boston.

Clinicians desire a test that complements anatomic imaging with CT and MRI or metabolic imaging with PET to determine if prostate cancer has spread.

Noninvasive tests rely on the diameter of the short axis of the lymph nodes to determine their status. On MRI, oval nodes less than 10 mm in diameter or round nodes less than 8 mm in size are labeled benign, whereas larger nodes of similar shape are considered malignant. However, Dr. Harisinghani said, "Size criterion is very inaccurate in staging lymph nodes."

During pelvic lymphadenectomy, surgeons generally sample the lower external iliac and obturator lymph nodes.

A study showed that when the dissection was extended to the higher external, internal, and common iliac lymph nodes as well as the presacral lymph nodes, the metastasis rate increased from 10% to 26% (J. Urol. 2002;167:1681-6).

But even an extended pelvic lymphadenectomy does not allow sampling of all nodes at the time of surgery, Dr. Harisinghani said at the symposium, cosponsored by the Society of Urologic Oncology and the American Society for Therapeutic Radiology and Oncology. Frozen section analysis of lymph node specimens also carries a false-negative rate of up to 30%, he added.

A new MRI technique involves the infusion of tiny, 20-nm-diameter, dextran-coated iron oxide spheres into the bloodstream. The spheres bind to macrophages in the lymph nodes. After 24 hours, nodal areas that did not take in the nanospheres indicate metastatic regions.

In 80 patients with advanced prostate cancer, the nanosphere imaging technique yielded significantly higher sensitivity (91% vs. 35%) and specificity (98% vs. 90%) as well as greater accuracy (97% vs. 76%) than conventional MRI alone in detecting metastases on a node-by-node basis (N. Engl. J. Med. 2003;348:2491-9). About 71% of the malignant nodes were below the size criterion, Dr. Harisinghani noted.

The imaging procedure allows surgeons to pinpoint positive nodes that they normally would not have dissected and to see exactly where they lie in relation to vessels, obturator nerves, and ureters. And by combining MRI data with data from CT scans, cancerous nodes can be targeted, thereby avoiding unnecessary radiation.

Clinicians also desire a test that complements anatomic imaging with CT and MRI or metabolic imaging with PET to determine if prostate cancer has spread to bone or soft tissue, Neil H. Bander, M.D, said in a separate presentation. Bone is the earliest and most common site of metastatic prostate cancer.

Second-generation monoclonal antibodies may offer the best hope for staging metastasizing or recurrent disease in prostate cancer patients, said Dr. Bander, professor of urologic oncology at Weill Medical College of Cornell University, New York.

Antibodies such as ^{111}indium-labeled J591 bind to the extracellular domain of prostate-specific membrane antigen (PSMA) on viable prostate cancer cells that express PSMA. PSMA is an integral membrane protein present in all prostate cancers.

In vivo imaging with J591 shows soft tissue and bone metastases of prostate cancer patients equally well. J591 imaging can detect bone metastases that go unseen in a standard bone scan, Dr. Bander noted.

Few clinicians still use imaging with the first-generation ^{111}indium-labeled monoclonal antibody Prostascint to PSMA to differentiate soft tissue metastases from bone metastases, he said.

Findings from clinical studies on Prostascint have shown that the antibody scan detects soft tissue metastases with greater accuracy than MRI or CT, but it does not detect bone metastases very well. ■

Digital Rectal Exam Still Identifies Prostate Cancer in Men With Normal PSA Levels

SAN ANTONIO — The digital rectal exam continues to play a critical role in identifying men with prostate cancer, according to a poster presentation by Joel Slaton, M.D., and Cesar Ercole, M.D., at the annual meeting of the American Urological Association.

Twenty-seven of 85 men (32%) with low prostate-specific antigen (PSA) levels and an abnormal digital rectal examination (DRE) had positive biopsies, reported Dr. Slaton and Dr. Ercole of the University of Minnesota, Minneapolis. Of those, 9 men (33%) were found to have high-grade tumors. The cancers would have been missed if the screening had relied on PSA alone.

The investigators attributed the false-negative PSA findings to tumors that were so poorly differentiated they underproduced PSA.

The study was a retrospective review of 3,817 prostate cancer screening visits between 1990 and 2000 where both DRE and PSA were performed. Of those, 81% of men had both a normal DRE and a normal PSA (defined as less than 4 ng/L). Those men did not undergo biopsy.

The remaining 719 men all had an abnormal DRE, a high PSA, or both, and all underwent biopsy; 240 of them (33%) were found to have cancer.

Of the 359 men with high PSA and abnormal DRE, 139 (39%) had positive biopsies, and slightly more than 20% had high-grade tumors. Of the 275 men with high PSA and normal DRE, 74 (27%) had positive biopsies, and about 20% had high-grade tumors.

—Robert Finn

Green Tea Extract May Prevent PIN Progression

BY ROBERT FINN
San Francisco Bureau

ANAHEIM, CALIF. — An extract of the catechins found in green tea appears to be effective in preventing the progression of high-grade prostatic intraepithelial neoplasia to invasive prostate cancer, Saverio Bettuzzi, Ph.D., reported at the annual meeting of the American Association for Cancer Research.

In the placebo-controlled, double-blind study, 30 men with prostatic intraepithelial neoplasia (PIN) took 200 mg of green tea catechins (GTCs) three times daily for 6 months. Another 30 men with PIN took a placebo.

Catechins are antioxidants, and they belong to a class of polyphenols called flavanols. Epigallocatechin-3-gallate (EGCG) is the major catechin in green tea, and in tissue culture EGCG has been shown to induce apoptosis in cancer cells, but not normal cells.

All the participants underwent biopsies at study entry and 6 and 12 months later.

At 12 months, nine (30%) of the men who took placebo had progressed to prostate cancer. Only one (3.3%) of the men who took GTC had progression of PIN to invasive cancer, for an apparent efficacy rate of 90%. The difference between the groups was statistically significant.

The participants were aged 5-75 years. Men who drank green tea, who were vegetarians, or who were taking antioxidants or antiandrogenic therapy were excluded from the study.

Dr. Bettuzzi, of the University of Parma (Italy), said that previous studies have shown that about 30% of men with PIN will typically progress to invasive prostate cancer within a year, the same rate as in the placebo arm of his study.

No serious adverse events occurred among the men taking GTCs.

The investigators measured levels of prostate-specific antigen (PSA) every 3 months during the course of the study. They noted no significant differences in PSA levels between the two groups.

GTCs were extracted in the laboratory, although Dr. Bettuzzi said that green tea extracts are also available commercially. The 600-mg daily dose of GTCs corresponds to about 12-15 cups of green tea daily. He said that 10-20 cups of green tea is the normal daily intake in China.

Dr. Bettuzzi said he had no financial conflicts related to the study, which was supported in part by Genprofiler GmbH, a company in Bolzano, Italy, that manufactures diagnostics for molecular biology. ■

Urine Leakage at Orgasm Common Postprostatectomy

SAN ANTONIO — Almost half of men who remain sexually potent after radical prostatectomy exhibit "climacturia"—leakage of urine at orgasm—according to a poster presented by Jason Lee, M.D., at the annual meeting of the American Urological Association.

In a consecutive cohort of 42 men who were at least 12 months post prostatectomy, 19 (45%) reported climacturia. Dr. Lee and his colleagues from Princess Margaret Hospital, Toronto, found no significant associations between climacturia and age, time since surgery, Gleason score, international prostate symptom score, urine flow rate, or the presence of incontinence.

Among the men experiencing climacturia, 4 (21%) said they experienced it rarely and 9 (47%) said they experienced it occasionally. Four others (21%) experienced climacturia most of the time or always.

Nine of the men (52%) said that the condition caused them significant bother, and 10 said it caused them nonsignificant bother. Four men (21%) said it caused their partners significant bother, and 15 (79%) said it caused their partners nonsignificant bother.

Leakage was only a few drops in 11 of the men, but 2 men said they leaked more than an ounce of urine, and a third man said he leaked more than 5 ounces.

Most of the men (16 of 19 [84%]) coped with their climacturia by voiding before intercourse. Two men additionally required a condom. Three men took no action.

The investigators concluded that climacturia is not uncommon following radical prostatectomy, and it should be discussed as a possible complication for men evaluating their treatment options.

—Robert Finn