ONCURA

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October 5, 2006

Via Federal Express

The Honorable Mark McClellan, M.D., Ph.D.
Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Attention: CMS-1506-P
Mail Stop C4-26-05
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: CMS-1506-P Medicare Program; Hospital Outpatient Prospective Payment System and CY 2007 Payment Rates; Proposed Rule

Dear Dr. McClellan:

The following comments are submitted on behalf of ONCURA,[1] a global leader in the minimally invasive management of prostate cancer. Oncura provides state-of-the-art brachytherapy source products. Since the early 1990's, ONCURA and its predecessor Amersham, have been committed to innovation in prostate brachytherapy. Our products include the ground breaking stranded brachytherapy source, RAPID Strand™ Iodine-125. RAPID Strand has benefited from extensive clinical experience and is the subject of numerous peer reviewed publications that have clearly and exclusively demonstrated its clinical value through the improved delivery of therapeutic radiotherapy, particularly in the treatment of prostate cancer.

We appreciate the opportunity to comment on the proposed rule published by the Centers for Medicare & Medicaid Services ("CMS") on August 23, 2006 *Federal Register* notice which proposes changes to the Hospital Outpatient Prospective Payment System (the "OPPS") for 2007.

We would like to thank CMS for the many refinements to the reimbursement methodologies that have been made in the past several years with regards to brachytherapy reimbursement since the inception of the HOPPS system. Although CMS has made some significant changes in brachytherapy payment policy, the Medicare Modernization Act and CMS' recent proposed rule highlight that further refinements are essential to ensure appropriate payment to hospitals and meaningful access to high quality cancer treatment for Medicare patients.

Oncura's Recommendations:

1. CMS should establish a new HCPCS codes for RAPID Strand™ (stranded) Iodine-125 sources in 2007.

[1] ONCURA was created in July 2003 by the merger of Amersham's brachytherapy business with Galil Medical Ltd's urology business.

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2. CMS should continue the current payment methodology for brachytherapy devices in the hospital outpatient setting (hospital's charges adjusted to cost for each device provided on a patient-by-patient basis) for all brachytherapy devices in 2007 and 2008.

3. CMS should include in the HOPPS final rule or the January 2007 HOPPS Medicare Program Transmittal clarification that the policy of billing all types of brachytherapy sources actually prescribed and ordered remains in force, notwithstanding the reference to "used" in the December 19, 2003 Program Transmittal.

4. CMS should implement mandatory code edits for brachytherapy procedure APCs 312, 313 and 651.

We set forth more detailed comments below.

* * *

1. OPPS BRACHYTHERAPY-NEW BRACHYTHERAPY SOURCE CODES

CMS should establish a new HCPCS code for RAPID Strand™ (stranded) Iodine-125 sources in 2007.

In the proposed rule, CMS invited the public to "submit recommendations for new codes to describe new brachytherapy sources in a manner reflecting the number, isotope and radioactive intensity of the sources." To that end, Oncura proposes the following new brachytherapy source code from our product offerings and urges CMS to implement this code on January 1, 2007:

1.) C26XX Brachytherapy device, RAPID Strand™ Iodine-125, per source

Significant concerns about the adequacy of CMS' data on brachytherapy devices were at the core of Congress' decision to enact Section 621(b) of the MMA in 2003. Similarly, ongoing concerns regarding CMS' data resulted in very recent recommendations from two Congressionally-created expert Advisory Panels to continue the current reimbursement methodology for brachytherapy devices.

As Congress highlighted in the MMA, one critical step in resolving these data problems is to ensure that CMS creates and uses separate codes for brachytherapy devices that reflect clinically-relevant distinctions among different types of brachytherapy devices. These codes should evolve over time.

However, CMS' current 2005 data does not reflect the clinical protocols that have emerged over the last decade resulting in increased clinical use of "stranded" brachytherapy devices for the treatment of prostate cancer. Specifically, the ground breaking RAPID Strand™ which has benefited from extensive clinical experience and is the subject of peer reviewed publications that have demonstrated its clinical value (See attachments 1-4).

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RAPID Strand™ brachytherapy sources are embedded into a custom braided suture material (polyglactin 90) and separated within the strand by material of an absorbable nature at specified intervals. This ensures the initial and long-term position of each source when implanted in and around cancerous tumors. RAPID Strand™ is manufactured **prior** to delivery to the customer and is not a process which can be performed by a hospital. The unique physical properties of the braided stranded suture support its ability to maintain position within the treated tissue and therefore RAPID Strand's proven ability to deliver improved radiation dosimetry (References 1 and 4). ,

In reviewing the age of the data used in the GAO's survey, the GAO noted that one brachytherapy professional society recommended that the data used to establish reimbursement rates should reflect the increased clinical use of stranded brachytherapy devices. The society highlighted that stranded brachytherapy devices are "more costly but considered clinically advantageous."[2] These observations underscore the need for a new code for RAPID Strand™.

RAPID Strand™ sources are distinct from traditional brachytherapy devices in a number of fundamental ways and as highlighted in the attached clinical articles (see attachments 1-4):

- As demonstrated in the clinical literature and widespread clinical practice, RAPID Strand™ sources improve patient safety and clinical outcomes in the treatment of prostate cancer.
- RAPID Strand™ sources require separate FDA clearances from traditional loose sources.
- RAPID Strand™ sources have increased costs of production arising from a number of factors, the material and labor costs associated with "stranding" the sources.

Of importance to note, RAPID Strand™ sources can be placed at the periphery of the prostate or outside the prostate gland, permitting treatment of extra-prostatic extension of the disease without the potential for migration into another body organ. Migration of traditional loose sources can occur, resulting in embolization of the sources to the lung or other critical organs.

RAPID Strand™ sources also meet CMS' longstanding definition of brachytherapy devices, as well as both the spirit and plain meaning of the coding and reimbursement provisions in Section 621(b) of the MMA. It is also worth noting that CMS has reflected differences in configurations of the same isotope before among the brachytherapy device codes established after the MMA (see the establishment of the code for linear Palladium-103).

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2 U.S. Gov't Accountability Office, *Rates for Certain Radioactive Sources Used in Brachytherapy Could Be Set Prospectively* (GAO-06-635, July 2006).

If a separate code for RAPID Strand™ sources existed in 2006, many thousands of Medicare's prostate cancer cases would already fall within each of these codes. Given the clinical benefits of using RAPID Strand™ sources in clinical practice, new codes are required to ensure that all Medicare patients have meaningful access to the safest and most effective treatment modalities in the future. Moreover, the absence of these codes has emerged as a primary barrier to further refinement of the reimbursement methodology for brachytherapy devices, especially the sources used to treat prostate cancer. In fact, distinct source APCs would enable the data collection and cost analysis necessary for appropriate refinement of the APC system. Having the additional stranded code would allow the hospitals to establish specific charges for the stranded products which would more accurately reflect the costs of both the loose Iodine-125 sources and the RAPID Strand™ sources.

To that end, Oncura proposes the following new brachytherapy source code and urges CMS to implement this code on January 1, 2007:

1.) C26XX Brachytherapy device, RAPID Strand™, per source

2. CMS should continue the current payment methodology for brachytherapy devices in the hospital outpatient setting (hospital's charges adjusted to cost for each device provided on a patient-by-patient basis) for all brachytherapy devices in 2007 and 2008.

There is significant variability in the number, radioactive intensities and types (configurations) of brachytherapy devices needed to treat individual cancer patients. Given this unique patient-to-patient variability, the use of prospectively-set average reimbursement runs the risk of creating significant barriers to access for individual cancer patients and placing financial pressures on hospitals to take shortcuts in the use of brachytherapy devices. Maintaining patient access to brachytherapy is critical, given that in many instances, brachytherapy devices provide the safest and most effective treatment for prostate and other forms of cancer.

Barriers to patient access are accentuated by the ongoing problems with CMS' data for brachytherapy devices. Further, CMS' codes for brachytherapy devices are not keeping pace with changes in clinical practice. Brachytherapy is a complex medical treatment that requires the implantation or application of devices that vary in numerous, clinically-important ways. These important clinical nuances must be factored into codes and payment to ensure that Medicare's policies reflect clinical treatment and patient access.

The proposed rule would change the way that brachytherapy devices are reimbursed by adopting prospectively-set average payment rates. As discussed below, the CMS proposal is based on data that are inaccurate, outdated and insufficiently detailed. In addition, CMS should continue the current reimbursement methodology for brachytherapy devices to satisfy the plain meaning and intent of Section 621(b) of the Medicare Modernization Act.

CMS should adhere to the recommendations of two congressionally-created Advisory Panels, which urged CMS to abandon the proposed rule and instead continue the current reimbursement methodology for brachytherapy devices

Shortly after CMS posted the proposed rule, two separate Congressionally-created public advisory groups recommended against proceeding with CMS' proposal to set fixed rates for brachytherapy devices.

- First, on August 24, 2006, the APC Advisory Panel recommended that CMS continue the current "charges adjusted to cost" reimbursement methodology for all brachytherapy devices in 2007 (instead of implementing CMS' proposal to begin prospectively-set payment rates in 2007).[3] The APC Advisory Panel based this recommendation on concerns about the validity of the data that CMS is using to calculate prospective payments for brachytherapy devices.

- Second, on August 28, 2006, the Practicing Physicians Advisory Council (PPAC) recommended that CMS "abandon" its proposed payment methodology for all brachytherapy devices under the hospital outpatient prospective payment system.[4] The PPAC also based its decision on concerns regarding CMS' data.

There are several additional points worth highlighting:

- These advisory panels, especially the APC Advisory Panel, are accustomed to working with imperfect data in establishing payment rates under Medicare. However, in this instance, the advisory panels identified the problems with CMS' brachytherapy device data as being so significant that CMS should not proceed with its August 23, 2006 proposal.

- Both advisory panels recommended continuation of the current "charges adjusted to cost" reimbursement methodology for **all** brachytherapy devices. CMS should not take a piecemeal approach to reimbursement for brachytherapy devices. Specifically, CMS should not attempt to apply prospective payment rates to a few (or any) types of brachytherapy devices. In the past, when CMS has taken a piecemeal approach to brachytherapy device reimbursement (applying one reimbursement methodology to some sources, but not others), tremendous and unnecessary confusion arose in the hospital community.

CMS should continue the current reimbursement methodology for brachytherapy devices for at least two more years to fulfill the brachytherapy provisions of the Medicare Modernization Act and because of the flaws in CMS' current data on these devices.

ONCURA continues to have significant concerns regarding the accuracy of hospital reported brachytherapy data on which CMS is basing the proposed payment for brachytherapy sources in 2007. As a member of The Coalition for the Advancement of Brachytherapy (CAB), we engaged Christopher Hogan, Ph.D. of Direct Research LLC to

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[3] Advisory Panel on Ambulatory Payment Classification (APC) Groups, *Panel Recommendations* (Aug. 23-24, 2006), available at: http://www.cms.hhs.gov/FACA/05_AdvisoryPanelonAmbulatoryPaymentClassificationGroups.asp.

[4] CMS, Practicing Physicians Advisory Council, available at: http://www.cms.hhs.gov/FACA/03_ppac.asp#TopOfPage.

perform an independent analysis of the 2005 hospital claims data that formed the basis for the 2007 payment rates. Dr. Hogan's analysis of the claims data was submitted under a separate cover in two letters submitted by CAB and we urge CMS to review the analysis as it points to the fundamental problems with CMS' current data for brachytherapy devices; including but not limited to the lack of separate data reflecting the use of RAPID Strand™ sources in clinical practice. Again, Congress highlighted in the MMA, one critical step in resolving the data problems facing CMS in the area of brachytherapy devices is for CMS to use separate codes that reflect clinically-relevant distinctions among different types of brachytherapy devices. These codes should evolve over time.

Another example of flawed claims data is with the high activity I-125 sources. Rank order anomalies exist in the proposed payments for brachytherapy devices. For example, High Activity Iodine-125 sources (C2634) always cost more than "low activity" Iodine-125 sources (C1718). In practice, High Activity sources typically are two to ten times more expensive than loose Iodine-125 sources. However, CMS' data do not reflect this fact, which indicates that CMS' data are inaccurate (see Table 1).

Table 1

HCPCS Code & Descriptor	Median Cost (2005 Hospital Claims)
C1718 Iodine-125	$35.54
C2634 High Activity Iodine-125	$25.77

ONCURA agrees with the Advisory Panels that maintaining the current reimbursement policy is the best course of action at this time, and we urge CMS to continue the current "charges adjusted to costs" (CCR) reimbursement methodology during 2007 and 2008.

The current methodology addresses the ongoing concerns regarding CMS' data on brachytherapy devices, especially during a period of evolution in the configurations and intensities used in clinical practice. Maintaining the current payment methodology will help physicians prescribe the most appropriate source and configuration for each patient. The current payment policy has been in place for more than two years and is working well for beneficiaries, hospitals and the Medicare program, ensuring patient access and allowing Medicare to be a prudent purchaser.

3. CMS should include in the HOPPS final rule or the January 2007 HOPPS Medicare Program Transmittal clarification that the policy of billing all types of brachytherapy sources actually prescribed and ordered remains in force, notwithstanding the reference to "used" in the December 19, 2003 Program Transmittal.

A December 19, 2003 Medicare Program Transmittal (Transmittal 32, Change Request 3007, Publication 100-20) appeared to instruct hospitals to bill for prostate brachytherapy sources used, while prior CMS policy has made clear that hospitals can bill for sources that the physician has actually ordered.

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Specifically, in the fall of 2001, CMS (then HCFA) issued on its Medlearn website Frequently Asked Questions, including the following:

> **Q. 114** Can hospitals bill for all brachytherapy seeds ordered by the physician even if the physician does not use all of the brachytherapy seeds?
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> **A. 114** Yes. There may be times when a physician orders more brachytherapy seeds than necessary since the physician may not know the exact amount of brachytherapy seeds needed for one patient. In this case, the hospital may bill for all of the brachytherapy seeds ordered.

We agree with this clarification. In fact, ASTRO has a coding corner Q & A guidance for its members (see http://www.astro.org/healthcare_economics/coding_corner/brachyseeds.htm) which states:

CODING QUESTION: An ASTRO member attended the 2004 ASTRO Socioeconomic Lunch and has the following question:

> For prostate seed implants, the member typically orders 6 extra seeds in addition to the preplan count. There was an ACR Bulletin back in December 2001 that said, "Therefore, it is valid that the hospital charge the "ordered seed" inventory for each patient, accounting for the seeds ordered only once." Is that still true? Should they bill for the number of seeds ordered or the number of seeds implanted in 2005?
>
> "The ASTRO Code Utilization and Application Subcommittee (CUAS) is not aware of anything that has changed in 2005 on this issue. It is presumed in the ACR statement on the seed inventory, that these extra seeds are either used, returned, or wasted--never transferred to another patient. Thus, it is appropriate for all seeds to be charged for, not just the ones that the doctor uses."

Oncura was concerned when CMS issued the January 2004 Hospital Outpatient Prospective Payment System Update that it could be misconstrued to restrict hospitals to only bill for seeds actually used (see section below which is underscored from December 19, 2003 Medicare Program Transmittal 32):

> January 2004 Update of the Hospital Outpatient Prospective Payment System (OPPS)
>
> "7. Payment for Prostate Brachytherapy In 2003, CMS paid a packaged amount for prostate brachytherapy. Hospitals were required to bill using HCPCS code G0256 (prostate brachytherapy with palladium sources), when palladium sources were implanted, and HCPCS code G0261 (prostate brachytherapy with iodine sources). These HCPCS codes were to be used in lieu of separate billing for CPT codes 77778 (interstitial radiation source application; complex) and 55859 (transperineal placement of needles or catheters into prostate for interstitial radiation element application, with or without cystoscopy), and HCPCS codes C1718 (iodine sources) and C1720 (palladium sources).

Under the OPPS for 2004, HCPCS codes G0256 and G0261 are deleted. For services furnished on or after January 1, 2004, hospitals are to use the CPT codes 77778 and 55859 to bill for the procedures and HCPCS codes C1718 and C1720 to bill for the brachytherapy sources. Separate payments will be made for the procedures and for the sources. Hospitals are to bill the brachytherapy sources showing the number of sources used in the units column. For example, if 100 brachytherapy sources are implanted in the prostate, the hospital will bill 100 units of the applicable code for the brachytherapy source."

This final section could be misconstrued by hospitals to limit billing to only prostate brachytherapy sources used, even if the physician prescribed in good faith what he/she believed to be necessary for the clinical needs of the patient, and the hospital, following the physician's prescription, purchased the prescribed number of sources. It is not uncommon for a treatment plan to be modified slightly in the operating room on the day of the implant. Physicians typically order extra sources for implant procedures so if the treatment plan must be altered during the course of treatment, or the physician determines a few extra sources are necessary to treat the patient, the additional sources are available to implant at the time of the procedure. In most cases, all ordered seeds are implanted leaving few that are left to decay. In either case, the hospital is required to absorb the cost of all the seeds ordered. Hospitals should not be penalized for following a physician's prescriptive order.

As a member of CAB, we sent formal correspondence to CMS on three separate occasions (April 27, 2005 to Don Thompson; May 20, 2004 to Cindy Read; and September 19, 2005 to Jim Hart) and requested clarification of this CMS policy in the hospital outpatient setting (see attachments 5-7). To date, neither CAB nor ONCURA has received a response from CMS to our letters or follow up emails regarding this issue.

4. *CMS should implement mandatory code edits for brachytherapy procedure APCs 312, 313 and 651.*

ONCURA continues to support mandatory reporting of all medical device "C" codes and related incentives to encourage hospitals to be more vigilant in reporting the total costs of performing device-related services. We recommend that CMS consider expanding their proposal to implement device code edits for all device-related and "device-dependent" APCs. Furthermore, we encourage CMS to accelerate its efforts to educate hospitals on the importance of accurate coding for devices and other technologies. Oncura was present at the August 2006 APC Advisory Panel meeting. At the APC Advisory Panel meeting on August 24 2006, the American Hospital Association (AHA), the Provider Round Table group and the APC Advisory Panel members who have oversight for coding agreed that requiring the appropriate device on the claim prior to processing and paying the claim was very helpful to the hospitals in terms of educating them on the appropriate device C-Codes that should be required for procedures, particularly the more complex procedures. In fact, the aforementioned groups agreed that the code edits are most helpful when the coding is complex. They stated that it often when the claims are return unpaid that they realize they have made coding errors. The complexity of the brachytherapy coding is clearly a challenge for the hospitals.

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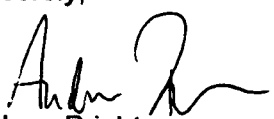
Brachytherapy requires the use of medical devices and we suggest that brachytherapy source "C" codes be required for APCs 312, 313, and 651. We believe that limited mandatory "C" coding is more of an administrative burden to hospitals and causes confusion. Since CMS requires C-Codes on the claims, putting the mandatory code edits in place is the next step toward obtaining more accurate claims data. We support expanding the 2007 policy to all device-related and "device-dependent" APCs to promote "correct coding" and to improve the quality of the claims data. In addition to using device "C" codes, hospitals should be educated on how to report charges for brachytherapy source devices utilized in the outpatient department.

In summary, Brachytherapy, and particularly RAPID Strand™, offers important cancer therapies to Medicare beneficiaries. Appropriate payment for brachytherapy sources is necessary to ensure that Medicare beneficiaries will continue to have full access to high quality cancer treatment in the hospital outpatient setting.

We hope that CMS will take these issues under consideration during the development of the 2007 Hospital Outpatient Final Rule. Should CMS staff have additional questions, please feel free to contact me at (484) 530-3922.

Thank you for your consideration.

Sincerely,



Andrew Bright
Vice President, Brachytherapy Americas

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ATTACHMENTS

1. Lee, William Robert et al. "Radioactive sources embedded in suture are associated with improved post implant dosimetry in men treated with prostate brachytherapy." Radiotherapy and Oncology 65 (2002): 123-127

2. Al-Qaisieh, Bashar et al. The use of linked seeds eliminates lung embolization following permanent seed implantation for prostate cancer. Int. J. Radiation Oncology Biol. Phys., Vol. 59, No. 2, pp. 397-399, 2004

3. Eshleman, MD, Jeffrey S. et al. Radioactive seed migration to the chest after transperineal interstitial prostate brachytherapy: extraprostatic seed placement correlates with migration. Int. J. Radiation Oncology Biol. Phys., Vol. 59, No. 2, pp. 419-425, 2004

4. Fagundes, Humberto M. et al. Transperineal TRUS-guided prostate brachytherapy using loose seeds versus RAPIDStrand: A dosimetric analysis. Brachytherapy 3 (2004) 136-140

5. April 27, 2005 Letter to Don Thompson

6. May 20, 2004 Letter to Cindy Read

7. September 19, 2005 Letter to Jim Hart

Coalition For The Advancement Of Brachytherapy

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April 27, 2005

Don Thompson
Director, Outpatient Care Division
Centers for Medicare and Medicaid Services
Mail Stop C4-01-27
7500 Security Boulevard
Baltimore, MD 21244-1850

Re: Clarification of Billing for Brachytherapy Sources

Dear Mr. Hart:

The Coalition for the Advancement of Brachytherapy (CAB) has been working with CMS for several years to assist in Medicare reimbursement policies on brachytherapy. This letter requests your assistance in clarifying a CMS Program Transmittal on billing for prostate brachytherapy sources in the hospital outpatient setting.

In brief, a December 19, 2003 Medicare Program Transmittal (Transmittal 32, Change Request 3007, Publication 100-20) appeared to instruct hospitals to bill for prostate brachytherapy sources used, while prior CMS policy has made clear that hospitals can bill for sources that the physician has actually ordered.

Specifically, in the fall of 2001, CMS (then HCFA) issued on its Medlearn website Frequently Asked Questions, including the following:

> Q. 114 Can hospitals bill for all brachytherapy seeds ordered by the physician even if the physician does not use all of the brachytherapy seeds?
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> A. 114 **Yes. There may be times when a physician orders more brachytherapy seeds than necessary since the physician may not know the exact amount of brachytherapy seeds needed for one patient. In this case, the hospital may bill for all of the brachytherapy seeds ordered.**

We agree with this clarification and were concerned when CMS issued the January 2004 Hospital Outpatient Prospective Payment System Update that appeared to restrict hospitals to only bill for seeds actually used (see section below which is underscored from December 19, 2003 Medicare Program Transmittal 32):

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This final section could be misconstrued by hospitals to limit billing to only prostate brachytherapy sources used, even if the physician ordered in good faith what he/she believed to be necessary for the clinical needs of the patient, and the hospital, following the doctor's order, purchased a higher amount. Hospitals should not be penalized for following a physician's order.

Thus, we would ask CMS in its next OPPS update to republish the 2001 Frequently Asked Question number 114, or otherwise clarify that the policy of billing all types of brachytherapy sources actually ordered remains consistent, notwithstanding the December 19, 2003 reference to sources "used".

Please feel free to contact Gordon Schatz, Esq. at (202) 414-9259 if you have additional questions. Thank you for your consideration. We look forward to hearing from you.

Sincerely,

Michael Krachon
Chair

Raymond Horn
Vice-Chair

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May 20, 2004

Cindy Read
Director, Outpatient Care Division
Centers for Medicare and Medicaid Services
Mail Stop C4-05-17
7500 Security Boulevard
Baltimore, MD 21244-1850

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Dear Ms. Read:

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September 19, 2005

James Hart
Director, Outpatient Care Division
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Centers for Medicare and Medicaid Services
Mail Stop C4-07-07
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Baltimore, MD 21244

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> January 2004 Update of the Hospital Outpatient Prospective Payment System (OPPS)
>
> "7. Payment for Prostate Brachytherapy In 2003, CMS paid a packaged amount for prostate brachytherapy. Hospitals were required to bill using HCPCS code G0256 (prostate brachytherapy with palladium sources), when palladium sources were implanted, and HCPCS code G0261 (prostate brachytherapy with iodine sources). These HCPCS codes were to be used in lieu of separate billing for CPT codes 77778 (interstitial radiation source application; complex) and 55859 (transperineal placement of needles or catheters into prostate for interstitial radiation element application, with or without cystoscopy), and HCPCS codes C1718 (iodine sources) and C1720 (palladium sources).
>
> Under the OPPS for 2004, HCPCS codes G0256 and G0261 are deleted. For services furnished on or after January 1, 2004, hospitals are to use the CPT codes 77778 and 55859 to bill for the procedures and HCPCS codes C1718 and C1720 to bill for the brachytherapy sources. Separate payments will be made for the procedures and for the sources. Hospitals are to bill the brachytherapy sources showing the number of sources used in the units column. For example, if 100 brachytherapy sources are implanted in the prostate, the hospital will bill 100 units of the applicable code for the brachytherapy source."

This final section could be misconstrued by hospitals to limit billing to only prostate brachytherapy sources used, even if the physician ordered in good faith what he/she believed to be necessary for the clinical needs of the patient, and the hospital, following the doctor's order, purchased a higher amount. Hospitals should not be penalized for following a physician's order.

Thus, we would ask CMS in its next January 2006 OPPS update to republish the 2001 Frequently Asked Question number 114, or otherwise clarify that the policy of billing all types of brachytherapy sources actually ordered remains consistent, notwithstanding the December 19, 2003 reference to sources "used".

Please feel free to contact Gordon Schatz, Esq. at (202) 414-9259 if you have additional questions. Thank you for your consideration. We look forward to hearing from you.

Sincerely,

Raymond Horn
Chair

Lisa Hayden
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Radioactive sources embedded in suture are associated with improved postimplant dosimetry in men treated with prostate brachytherapy

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Abstract

Background and purpose: Reports using the retropubic and transperineal technique of prostate brachytherapy suggest that adequate radiation doses are required for good clinical results with I-125. After 3 years of using loose sources (LS), radioactive sources embedded in suture (SES) were introduced into our prostate brachytherapy technique. The purpose of the present report is to determine whether dosimetric quantifiers of implant adequacy were affected by the use of SES.

Materials and methods: Between September 1999 and April 2000, 20 patients were treated with prostate brachytherapy alone with a preplanned, preloaded needle technique using LS. Between May 2000 and February 2001, 20 patients were treated with prostate brachytherapy alone with a preplanned, preloaded needle technique using SES. Dosimetric quantifiers (DQ) of implant adequacy were calculated using a computed tomography scan performed 1 month following prostate brachytherapy. DQ were compared between patients treated with LS and patients treated with SES.

Results: The demographic characteristics were similar for each group. Men treated with SES had slightly smaller prostate glands compared to men treated with LS. The mean total activity and activity per seed were similar for each group but the activity per unit volume was slightly higher for the SES group. Patients treated with SES were found to have significantly improved DQ compared to patients treated with LS. The mean V100 for patients treated with SES was 94.10% compared to 86.54% in those patients treated with LS ($P < 0.001$).

Conclusions: In our experience using preplanning and preloaded needles, the use of SES is associated with improved postimplant DQ.

Keywords: Prostate cancer; Interstitial brachytherapy; Iodine 125

1. Introduction

Prostate cancer is the most commonly diagnosed solid tumor in American men. In 2001, approximately 198 100 new cases will be diagnosed [10]. A majority of these cases will be clinically organ confined at the time of diagnosis [10]. The management of organ-confined adenocarcinoma of the prostate remains one of the most controversial areas in all of oncology. Treatment options include expectant management, radical prostatectomy, external beam radiation therapy, and interstitial brachytherapy [2]. In the absence of prospective randomized trials, proponents of each technique continue to aver that one therapy is superior to all others.

Prostate brachytherapy (PB) has been used for many decades with heterogeneous results [6,8,15,22]. Improvements in technology have allowed the development of a transperineal approach in which radioactive sources can be placed accurately within the prostate gland using real time ultrasound guidance [6]. Excellent results have been reported with the use of brachytherapy alone in men with favorable risk disease, and brachytherapy combined with external beam radiation therapy in men with intermediate risk prostate cancer [6,7,8,15].

With the development of sophisticated treatment planning systems, it is now possible to obtain three-dimensional dosimetric evaluations soon after PB is completed [5,13]. The American Brachytherapy Society has recommended that all patients treated with PB undergo some form of dosimetric analysis following treatment [13]. This is most commonly achieved with a pelvic computed tomography (CT) scan performed within weeks after prostate brachytherapy. A number of dosimetric quantifiers (DQ) have been studied and reported. The two DQ that have been most closely studied include V100 and D90 [13,18–20]. V100 represents the percentage of the prostate volume

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that receives 100% of the prescription dose. D90 is the maximum dose received by 90% of the prostate gland.

A seminal report from the largest reported series using retropubic seed placement observed that the prescription dose often was not achieved because of inaccurate seed placement [9]. Importantly in this report, lower prostate doses were associated with inferior outcomes, especially local relapse. The few patients that received homogeneous high doses to the prostate gland achieved excellent local control rates.

A recent report of patients treated with a modern transperineal ultrasound-guided technique also reports a dose response relationship [20]. In this series all patients underwent postimplant dosimetric analysis using CT scans obtained approximately 1 month following prostate brachytherapy. Those patients found to have a D90 of greater than 140 Gy experienced improved disease-free survival when compared to patients found to have a D90 of less than 140 Gy. This data with modern technique supports the notion that disease control is associated with dosimetric parameters that can be easily measured. A technique that increases the likelihood of achieving adequate radiation dose of the prostate gland should result in improved disease control.

Although many different techniques are utilized during prostate brachytherapy, most patients are treated with loose sources (LS). A unique medical device that consists of loose seeds embedded in stiffened suture has been developed (RAPIDStrand™, Nycomed Amersham, United Kingdom). This formulation allows for the placement of sources outside of the prostate gland without the concern of seed migration that has been documented with loose seeds [21]. The fixed geometric distribution of seeds embedded in suture (SES) reduces spacing errors and may allow for improved dose delivery [16].

After approximately 3 years of performing prostate brachytherapy at Wake Forest University using LS, we incorporated SES into the prostate brachytherapy procedure. The purpose of this analysis is to determine if the use of SES is associated with improved DQ compared to the use of LS.

2. Materials and methods

2.1. Brachytherapy technique

Transperineal prostate brachytherapy at Wake Forest University began in September 1997. The technique has been previously described by Blasko and Grimm [6]. This technique relies on preplanning using an ultrasound volume study of the prostate gland. Based on the preplan sources are ordered and preloaded into brachytherapy needles using catgut spacers to ensure adequate spacing between sources. From September 1997 until April 2000, all men were treated with LS. In May of 2000, SES were incorporated into the brachytherapy procedure. The needles containing SES were confined to the periphery of the prostate gland. LS were utilized in the center of the prostate gland. On average for a SES implant, 70–80% of the sources were SES. This technique differs from that of Batterman and others where SES are used throughout the gland [4]. All patients were treated with I-125 alone and the prescription dose was 144 Gy.

2.2. Dosimetric evaluation

According to a uniform institutional protocol, 1 month following prostate brachytherapy, all men underwent a CT scan of the pelvis and prostate. Three millimeter thick images were obtained at 3 mm scan intervals from 2 cm above the most superior seed to 2 cm below the most inferior seeds. The images were then transferred by local area network to the Treatment Planning System. Prostate volumes were outlined by single radiation oncologist (WRL). A single physicist localized each individual seed on the CT scan, and isodose volumes were calculated. Dose volume histograms were calculated with 0.5 mm pixel spacing, the voxel size was 1.25 cc and the dose bins were 5 Gy. A variety of DQ were examined to allow comparison between the patients treated with LS and those treated with SES. At the recommendation of the American Brachytherapy Society, we have reported the V100 and D90 [13]. The rate of seed migration was determined by a KUB film and chest X-ray taken 1 month following the implant procedure.

2.3. Statistical analysis

Descriptive analyzes were performed using PCSAS Version 6.12. Comparison of categorical variables relied on the chi-square test and continuous variables were compared using the t-test. The assumptions of these tests were met and no transformations were required. All P values are two-sided.

3. Results

The patient and treatment characteristics for the entire study population are listed in Table 1. The characteristics are also sorted according to implant technique (LS versus SES). None of the demographic characteristics are significantly different between the LS and SES groups. Men treated with SES did have slightly smaller prostate glands on average than men treated with LS (SES 33.74 cc, LS 39.55 cc; $P = 0.0474$). The treatment parameters were similar for each group although the SES group did have a significantly higher activity per unit volume of prostate (LS 0.92 mCi/cc, SES 1.02 mCi/cc, $P = 0.0091$). Seed migration was observed in two (10%) patients treated with LS. Seed migration was not seen in any patients treated with SES.

Table 2 lists the dosimetric quantifiers of implant

Table 1
Patient and treatment characteristics of the overall study population ($n = 40$) and stratified by implant technique[a]

Variable	Overall ($n = 40$)	LS group ($n = 20$)	SES group ($n = 20$)	P-value
Mean age (SD)	65.8 (5.4)	66.65 (5.3)	65 (5.6)	NS
T1 (%)	29 (72)	14 (70)	15 (75)	NS
T2 (%)	11 (28)	6 (30)	5 (25)	
Mean pPSA (ng/ml)	6.44	6.43	6.44	NS
Gleason 2–6 (%)	37 (92)	18 (90)	19 (95)	NS
Gleason 7 (%)	3 (8)	2 (10)	1 (5)	
Mean (SD) prostate volume (cc)	36.6 (9.3)	39.55 (10.7)	33.74 (6.9)	0.0474
Mean (SD) activity/source (mCi)	0.36 (0.03)	0.35 (0.02)	0.36 (0.03)	NS
Mean (SD) total activity (mCi)	34.77 (6.0)	35.16 (5.88)	34.39 (6.3)	NS
Mean (SD) activity/volume (mCi/cc)	0.97 (0.14)	0.92 (0.14)	1.02 (0.11)	0.0091

[a] SD, standard deviation; NS, not significant; and $P > 0.05$.

adequacy for the entire group and stratified by implant technique. By any measure, those patients treated with SES were found to have significantly improved dosimetric coverage of the prostate gland. The mean V100 for those patients treated with SES was 94.10 versus 86.54% in those patients treated with LS ($P < 0.001$).

4. Discussion

As the utilization of PB increases in the United States, there is accumulating evidence that treatment success is dependent on the accurate delivery of an adequate radiation dose to the prostate gland. The wide availability of robust treatment planning systems should allow most practitioners to obtain measures of implant quality in a timely fashion. This information should allow clinicians to modify their technique, if needed, resulting in improved dosimetric outcomes. We have used a rigorous dosimetric analysis to examine whether the incorporation of SES into our technique improves postimplant DQ. Our results indicate that the use of SES is associated with improved DQ as defined by CT scan 1 month following PB. Based on this analysis, we have moved to using SES for all subsequent implants.

A number of other investigators have utilized postimplant DQ to examine whether changes in technique or equipment result in improved dosimetric outcomes [3,18,23]. These modifications in technique or equipment run the gamut from the simple to the complex. Baird et al. observed that placing two marker seeds prior to PB (one at the base and another at the apex) resulted in better D90 values [3]. Stock et al. found that the use of a dual-phase ultrasound probe resulted in fewer patients with low D90 values compared to the use of a mechanical sector probe [18]. Zelefsky et al. at Memorial Hospital in New York have found that intraoperative computer-optimized conformal planning is associated with improved dosimetric outcomes [23]. It is the authors' opinion that SES is a treatment improvement device which, like the other examples listed above, can lead to better postimplant dosimetry.

This association between SES and improved implant dosimetry is quite plausible. In two large reports examining the spatial distribution of dose with the prostate gland, the region of the prostate most likely to receive a lower dose is the anterior base [14,17]. This region is close to the dorsal vein complex and sources placed near the anterior base could be more prone to embolize through the venous system. There is evidence that the use of SES results in lower rates of source embolization [21]. In this small sample the rate of seed embolization was lower with SES but the sample size is quite small and this difference was not statistically significant. We are presently examining the rate of source migration in a larger group of patients. Since the base is at the periphery of the implanted volume the migration of a few sources can result in significant unintended underdosage. One possible explanation of our results could be that SES allows for less source embolization, which is particularly important at the base, resulting in improved target coverage. It is important to point out that the use of loose seeds in the central portion of the prostate gland does not appear to result in seed embolization (no embolization seen in 20 patients treated with SES). Unlike the reports of

Table 2
Dosimetric quantifiers for the overall study population ($n = 40$) and stratified by implant technique

Variable	Overall ($n = 40$)	LS ($n = 20$)	SES ($n = 20$)	P-value
Mean (SD) V100 (%)	90.32 (5.1)	86.54 (3.7)	94.10 (2.9)	< 0.001
Mean (SD) V90 (%)	93.53 (4.2)	90.43 (3.2)	96.63 (2.2)	< 0.001
Mean (SD) V80 (%)	96.31 (3.0)	94.12 (2.6)	98.50 (1.3)	< 0.001
Mean (SD) D90 (Gy)	148.17 (21.9)	132.13 (11.6)	164.2 (17.3)	< 0.001
D90 >140 Gy (%)	27 (67)	7 (35)	20 (100)	< 0.001

others, we did not systematically identify the regions that were underdosed. We are in the process of performing sector analysis in a larger group of patients. At present it is our opinion that in the majority of cases the base region is more likely to be underdosed.

At least three criticisms of this analysis deserve mention. First, this is a non-randomized retrospective comparison. All patients in this report were treated by the same PB team including a single radiation oncologist and a single urologist. Other than changing the type of source used for the procedure all other variables have remained the same. We chose to compare the SES group with the most recent 20 LS cases rather than the entire LS experience because we have documented a steep learning curve for this procedure and we were seeking to minimize any temporal trends [11]. There are small differences in the prostate size and the activity per unit volume implanted between the SES and LS groups. It is possible that a 10% increase in activity will improve the V100 and D90 by 2–3% but the magnitude of improvement we observed was larger than this. These variables were included in the multivariate analysis and the source type continued to be the only independent predictor of implant quality. As much as the investigators have attempted to keep all variables constant, the potential for residual confounding exists.

Secondly, one may question the use of an intermediate endpoint such as V100 or D90. As has been previously mentioned, limited information does suggest that measures of implant adequacy can be correlated with disease-free survival. The authors hasten to point out, however, that no measure of implant adequacy has been associated with overall survival or prostate cancer specific survival. The correlation between some measure of radiation dose to the prostate gland and survival (if one exists) can only be examined in large cohorts of patients with long follow-up. In the meantime, there is evidence that the DQ used in this report are reliable [5,18]. The authors believe that DQ can provide clinicians with important information that can be utilized as part of a continuous quality improvement process to maximize the likelihood of an adequate prostate implant.

Finally the DQ used in this report rely on prostate delineation on the postimplant CT scans. There are two reports that indicate that there is a large amount of disagreement between reviewers when different reviewers are asked to outline the prostate on identical images [1,12]. In this report, the prostate was outlined by a single reviewer (WRL) so interobserver reliability was not a factor in prostate delineation. The single reviewer was not aware of the technique used (LS versus SES) in each case.

5. Conclusions

This non-randomized retrospective comparison of transperineal preplanned prostate brachytherapy indicates that the use of SES results in improved postimplant dosimetry compared to the use of LS.

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THE USE OF LINKED SEEDS ELIMINATES LUNG EMBOLIZATION FOLLOWING PERMANENT SEED IMPLANTATION FOR PROSTATE CANCER

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CLINICAL INVESTIGATION **Prostate**

THE USE OF LINKED SEEDS ELIMINATES LUNG EMBOLIZATION FOLLOWING PERMANENT SEED IMPLANTATION FOR PROSTATE CANCER

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Purpose: A number of reports of ^{125}I seed migration to the lungs after prostate brachytherapy have been published. There are, however, very limited data available on how to reduce the risk of this event. The purpose of the present report is to determine whether seed embolization to the lungs can be minimized by using stranded seeds alone for brachytherapy.

Methods and Materials: Between December 2001 and December 2002, 238 patients with early prostate cancer were treated with prostate brachytherapy as monotherapy using ^{125}I stranded seeds (RAPIDStrand) exclusively. All patients had fluoroscopy during the implant and immediate postimplant radiographs of the pelvis. A sample of 100 patients had chest radiographs performed, on average, 55 days after implant. To determine the ease, or lack of ease, with which these ^{125}I seeds could be visualized, 4 patients who did not have prostate cancer and who were having routine chest radiographs as part of their management for other cancers consented to have posteroanterior and lateral radiographs performed with inactive ^{125}I seeds taped to the skin of the thorax. All radiographs were reviewed by a single radiologist.

Results: The number of seeds noted on the postimplant radiographs corresponded to the number of implanted seeds in all 238 cases: There was, therefore, no evidence of seed embolization immediately postimplant. On review of the 100 chest radiographs, no embolized seeds were found.

Conclusion: No evidence of seed embolization was observed with the use of stranded ^{125}I seeds as used for prostate brachytherapy. © 2004 Elsevier Inc.

Prostate, Brachytherapy, Iodine-125, Migration, Pulmonary embolism.

INTRODUCTION

Prostate brachytherapy is an increasingly popular method of treatment for early-stage prostate cancer. Current seed implantation technique is generally based on peripheral loading (1–3) to reduce the dose to the urethra. This technique often requires seeds to be implanted adjacent to the prostatic margin, which may be associated with seed embolization to the lungs (3–16).

Steinfeld *et al.* (11) were the first to report pulmonary seed embolization after prostate brachytherapy. The likely explanation is that an ^{125}I seed (4.5 mm in length and 0.8 mm in diameter) is small enough to migrate through the dense venous plexus surrounding the prostate. Seeds entering the venous system access the right heart and then embolize and become lodged in the lungs (3). Seed migration to other sites has been reported (17, 18) and is most likely explained by the presence of a right-to-left intracardiac shunt.

There have been a number of literature reports addressing the risk of seed embolization (19–21). The aim of this study was to investigate the incidence of ^{125}I seed embolization with stranded seeds only (RAPIDStrand).

METHODS AND MATERIALS

Transperineal prostate brachytherapy at Cookridge Hospital began in 1995 and, to date, over 1100 implants have been performed. Implant techniques have evolved over the years, but in essence are still based on the preplan method. Between 1995 and September 1999, all patients were implanted with ^{125}I free seeds. After this, RAPIDStrand was introduced. Initially, these stranded seeds were restricted to needles placed at the periphery of the prostate with no extracapsular placement. The periurethral areas were implanted with free seeds. Since December 2001, RAPIDStrand has been used exclusively for all our prostate implants.

Between December 2001 and December 2002, 238 pa-

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lanted. The average treated prostate volume nge, 11.7–54.0 cc). The average number of d was 81 (range, 44–115 seeds) with average 60 U (range, 0.413–0.492 U) loaded into an needles (range, 20–40 needles) to deliver a se of 145 Gy (1, 2).

s had fluoroscopy during the implant as per dure for this institution. One hundred consec- s had chest radiographs (posteroanterior [PA]), on average 55 days after implant (median, 53 e, 24–115 days). These radiographs were re- a single radiologist (B.C.), who is familiar with rachytherapy.

atients who did not have prostate cancer consented hest radiographs to act as a reference group. None 4 patients had any known chest pathology but did chest radiography as part of their management. The e of this was to explore the ease of visualization of eds on PA and lateral chest radiographs. Inactive ^{125}I were taped to various parts of the chest wall, and the of identification was noted over different tissues (lung nchyma, heart, spine, and ribs).

RESULTS

(*A*) The seed count on immediate postimplant pelvic radiographs equated to the number of implanted seeds in all 238 patients. There was, therefore, no evidence of seed loss immediately after the implant. (*B*) No evidence of seed embolization to the lungs was observed on the sample of 100 consecutive chest radiographs. (*C*) Seeds were clearly visible on all 4 control patients—both PA and lateral projections.

DISCUSSION

In common with other groups, we did occasionally observe seed embolization to the lungs with the use of free ^{125}I seeds. The clinical consequences relating to these embolized seeds were considered negligible—the main concern was the reduction in the number of seeds contributing to dose in the prostate gland itself. The introduction of stranded seeds (22) was considered an advantage by our group and was therefore incorporated into our brachytherapy technique. Stranded seeds have been reported to improve the implant dosimetry (23), as well as reduce the possibility of seed embolization from 11.6% to 0.7% compared to free seeds (3). The results of our study suggest that the exclusive use of RAPIDStrand seeds may eliminate the risk of seed embolization to the lungs.

RAPIDStrand was initially used in our center in conjunction with a few free seeds that were implanted around the urethra. This technique was adopted to avoid excess preurethral dosage. Free seeds were loaded in brachytherapy needles using spacers that left sufficient gaps between free seeds, as planned. Recently, this technique has been replaced by one using only linked seeds for the whole implant. To maintain an acceptable urethral dose, a split needle method was introduced. For example, if a plan produces a single needle containing 2 seeds at 0.0-mm retraction from the base and another 2 seeds at 40.0-mm retraction, this needle is divided into 2 needles (splits). The first needle contains 2 linked seeds to be implanted at 0.0-mm retraction, and the second needle contains another 2 linked seeds to be implanted at 40.0-mm retraction using the same coordinate on the ultrasound template. This method may increase seed fixity and, hence, improve dosimetry and eliminate seed migration, as well as avoid an excessive urethral dose.

RAPIDStrand is ^{125}I seeds linked by a braided, tissue-absorbable suture material made of Polyglactin 910. Experimental i.m. implantation studies of Polyglactin 910 show absorption begins as a loss of tensile strength followed by a loss of mass. The suture material retains approximately 75% of the original tensile strength at 2 weeks postimplantation. All of the original tensile strength is lost between 4 and 5 weeks postimplantation. Absorption is essentially complete between 56 and 70 days (RAPIDStrand instructions for use). The seeds, however, should be well epithelialized within the gland by this time, and so migration and embolization are unlikely to occur even after suture absorption. Our study supports this view with no evidence of any seed embolization observed.

Visualization of ^{125}I seeds on chest radiographs might be influenced by a number of factors. If the seed is lying behind high-attenuation regions, such as bony structures or the heart, it might be less visible on the chest radiographs. ^{125}I seeds are, however, very radiopaque (silver and titanium shell), and there was no problem identifying these seeds on the chest radiographs of the control patient group, regardless of site or radiographic projection. Furthermore, all chest radiographs were reviewed by an experienced radiologist familiar with prostate brachytherapy, who had the specific purpose of identifying seeds. We do not consider, therefore, that seeds could have been overlooked or rendered inconspicuous in our study.

CONCLUSION

The exclusive use of stranded seeds for prostate brachytherapy is associated with a negligible risk of seed embolization to the lungs. This should minimize any detrimental effect on prostate dosimetry resulting from possible seed loss, as well as eliminate any potential risk of radiation toxicity to organs affected by seed embolization.

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Transperineal TRUS-guided prostate brachytherapy using loose seeds versus RAPIDStrand: A dosimetric analysis

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Transperineal TRUS-guided prostate brachytherapy using loose seeds versus RAPIDStrand: A dosimetric analysis

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ABSTRACT

PURPOSE: An analysis of the effect of stranded ^{125}I and loose (predominantly ^{103}Pd) sources on dosimetric outcomes of brachytherapy of the prostate.

METHODS AND MATERIALS: Between September 1998 and December 2003, 473 patients were treated with brachytherapy for biopsy-proven carcinoma of the prostate. Of these, 337 (71%) procedures were performed using free seeds placed with a Mick applicator. Beginning in April 2002, a program of stranded ^{125}I sources (RAPIDStrand) was implemented; 136 (29%) patients were treated via this approach. Dosimetric variables were collected, as were events of urinary retention.

RESULTS: Mean V100 values for the stranded ^{125}I approach were greater than those for free seeds ($p < 0.0005$), whether ^{125}I or ^{103}Pd ($p < 0.005$). Use of the strand was the most significant determinant of V100 of all variables examined. The stranded ^{125}I approach was also associated with higher mean D90 values and lower V150-urethral doses.

CONCLUSIONS: Use of stranded ^{125}I was associated with superior dosimetric outcomes in this group of patients.

Keywords: Prostate cancer; Brachytherapy; Dosimetry; V100; D90

Introduction

Prostate cancer is the most commonly diagnosed malignancy in American men, with an estimated 220,900 new cases in 2003 (1). Since the introduction of PSA screening, a growing number of patients will be diagnosed with organ-confined disease (2). The well-established treatment options for patients with early disease include radical prostatectomy, external beam radiation, or prostate brachytherapy (3). In the absence of a prospective randomized trial, retrospective studies have shown these therapies to provide comparable cure rates (4–11).

Transperineal prostate brachytherapy is a complex procedure that can be performed via a number of different approaches. This variety in technique arises from several factors, including the method of seed delivery (applicator or pre-loaded needle), the nature of implanted sources (individual, stranded, linked), and the planned distribution of the radiation dose. Several seed delivery techniques and dosimetric philosophies are currently described in the literature (12–25).

Our program started in 1998, using a technique employing loose seeds delivered with the Mick applicator (Mick Nuclear, Bronx, NY). In March of 2002, we modified our technique to employ suture-embedded radioactive sources (RAPIDStrand; Oncura, Plymouth Meeting, PA) delivered by pre-loaded needles using the Utrecht University method described by Battermann *et al.* (25). The objective of this study is a comparison of the postprocedure dosimetric outcomes resulting from the two distinct approaches.

Methods and materials

Our ultrasound-guided transperineal prostate brachytherapy program began in September 1998. All cases involved preplanned methodology, where a transrectal ultrasound

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(TRUS) volume study serves as the basis for a treatment plan, which is carried out in the operating room.

A total of 473 patients with localized prostate cancer were treated between September 1998 and December 2002.

Technique 1

The technique used from September 1998 through March 2002 employed loose seeds placed with a Mick applicator (26, 27). Three hundred thirty-seven patients were treated with this technique. Of 337 patients, 28 (8%) received loose ^{125}I (0.32 mCi/seed, 0.425 U) whereas 309 (92%) patients received ^{103}Pd [NIST 99, 2.15 U (28)]. The prescription dose was 145 Gy for ^{125}I patients treated with monotherapy and 120 Gy when combined with external beam radiation. Prescription doses for ^{103}Pd patients were 125 Gy (pre-NIST 99, 115 Gy) for monotherapy and 100 Gy (pre-NIST 99, 90 Gy) for the combined modality.

Technique 2

Beginning in April 2002, we changed our technique to employ ^{125}I RAPIDStrand as described by Battermann (25). RAPIDStrand consists of ^{125}I sources embedded in a dried vicryl suture material. Approximately 80–85% of the seeds placed in the prostate were stranded, while 15–20% were placed as loose seeds, primarily to cover the base and apex around the urethra. The sources consisted of 0.33/0.34 mCi, 0.425 U ^{125}I RAPIDStrand for both monotherapy and combined modality. One hundred thirty-six patients were treated by this technique. Planned doses were identical to that of the earlier, free seed ^{125}I cases.

In all cases a peripherally weighted plan was used, in which 75–80% of seeds were placed in the periphery of the prostate gland. The clinical target volume (CTV) included the prostate gland as defined by the TRUS volume study images and the planning target volume (PTV) included a 5 mm margin around the CTV with the exception of the posterior aspect of the prostate, where the margin was minimal.

Both techniques were similar with regard to the surgical implant. On the day of the implant patients were brought into the operating room and placed either under general or spinal anesthesia. Patients were positioned in the lithotomy position and the rectum was suctioned. The perineum was scrubbed with betadine and a Foley catheter was placed with 50 cc contrast instilled into the bladder. The Foley was clamped and a C-arm X-ray unit was positioned over the pelvis. The perineum was dried and a scrotal drape was attached. A TRUS probe was inserted into the rectum and attached to the stand and stepping unit along with the template. Once the images reproduced the original volume study images, that is, aligning the prostate gland with the previous prostate volume study images, insertion of sources according to the pre-plan commenced. Extra seeds were placed at the end of the procedure at the discretion of the radiation oncologist. The Foley catheter remained in place until the completion of a CT scan either the same day or the morning following the procedure. As recommended by the American Brachytherapy Society (29), postimplant dosimetric parameters were quantified including V100, V150 prostate, V150 urethra, and D90.

Differences between the dosimetric parameters using loose seeds and RAPIDStrand were evaluated using a general linear model method (GLM; SPSS Inc., Chicago, IL), specifically a linear regression analysis solving for V100.

Results

Patient characteristics are outlined in Table 1. Given the relatively short follow-up interval, disease-free and overall survival data will not be addressed in this article.

Dosimetric outcomes as determined by 24-h CT-based postplan analysis are listed in Table 2. The observed V100 was significantly greater for the ^{125}I RAPIDStrand patients (mean, 92.5%; n = 136) than for the loose seed patients (mean, 88.4%; n = 336), $p < 0.005$ by independent samples t-test (Fig. 1).

The mean V100 for RAPIDStrand (92.5%) was significantly greater than both loose ^{125}I (78.8%) and loose ^{103}Pd (89.3%) seeds, $p < 0.005$ by F-test (Fig. 2).

Linear regression analysis solving for V100 using strand versus no strand, isotope (^{125}I versus ^{103}Pd), and type of therapy (implant combined with external beam versus implant monotherapy) revealed RAPIDStrand as the most powerful determinant of V100 in this series ($p < 0.005$, partial $h^2 = 0.12$, Table 3). Preimplant prostate volume, administration of antiandrogen therapy, and age were included in the regression and found to be insignificant.

The mean D90 for RAPIDStrand cases was significantly greater than that of ^{103}Pd free seed cases, whereas the mean V150-prostate and V150-urethra were lower (Table 2). No data on these parameters was available for the ^{125}I free seed cases.

Table 1
Patient characteristics

Presenting serum PSA	n (%)	Gleason sum	n (%)
0–9.9 ng/ml	409 (86)	2–4	3 (1)
10–19.9 ng/ml	48 (10)	5–6	322 (68)
>20 ng/ml	13 (3)	7	126 (27)
none	3 (1)	8–10	19 (4)
		none	3 (1)

Clinical stage	n%
T1a/b	1 (–)
T1c	257 (54)
T2a	176 (37)
T2b	17 (4)
T2c	10 (2)
T3a	4 (1)
none	8 (2)

Table 2
Dosimetric parameters by treatment type

	n	Mean V100 (SD)	Mean D90[1] (SD)	Mean V150 (SD)	Mean V150-U (SD)
Free ^{103}Pd	309	89.3 (7.7)	103.4[2] (17.2)	59.8 (12.3)	9.8 (15.0)
Free ^{125}I	28	78.8 (12.9)	not done	not done	not done
RAPID Strand ^{125}I	136	92.5[3] (5.9)	108.8[3] (13.0)	46.5[3] (12.1)	3.6[3] (8.6)

[1] Normalized to prescription dose.
[2] n = 284.
[3] $p < 0.005$ vs. other treatment(s).

The rate of retention for free ^{125}I was 1/27 (3.6%), for free ^{103}Pd 30/309 (9.7%), and for RAPIDStrand 4/136 (2.9%). These differences were significant (exact p = 0.01).

Discussion

Several authors have compared postimplant dosimetry using loose versus suture-embedded seeds. Battermann (25) reported the Utrecht University experience using loose and stranded ^{125}I. Based on a series of 249 patients, he noted an increase in mean coverage from 55–68% of the prostate volume with loose seeds to 90% with RAPIDStrand. In addition, the reported seed migration dropped from 10% to 1–3% following the implementation of stranded seeds.

Lee *et al.* (17) used loose sources for 3 years before changing to embedded ^{125}I seeds. Patients treated with suture-embedded seeds were found to have significantly improved dosimetric coverage of the prostate gland. In that series, the observed mean V100 was 94.1% versus 86.54% for the patients treated with loose seeds ($p < 0.001$).

Fagundes *et al.* (30) reported dosimetric results from Porto Alegre, Brazil using the Mick applicator with loose ^{125}I and RAPIDStrand. They noted an improvement in the V100 from 82.8% with loose seeds to 93.6% with RAPIDStrand.

The present series revealed a statistically significant improvement in the dosimetry when RAPIDStrand was used. The observed V100 improved from 88.4% to 92.5% based on postimplant CT scan done within 24 h following implementation of RAPIDStrand. Since this series includes patients treated by free ^{125}I, free ^{103}Pd, and stranded ^{125}I, we are able to show a greater V100 for RAPIDStrand cases than both free ^{103}Pd and free ^{125}I cases. Likewise, upon regression analysis, while both isotope and implant dose (for boost or primary therapy) are significant factors for V100, the use of RAPIDStrand retains significance as a predictor in the final model (Table 3).

Patients implanted by the RAPIDStrand technique also experienced less acute urinary retention: 8.9% with loose seeds versus 2.9% with RAPIDStrand (p = 0.01). This decline in urinary retention correlated with a lower V150 urethra, 9.7% versus 2.8%. However, given the lack of detailed dosimetry data for the early loose ^{125}I cases, we are unable to attribute this difference unequivocally to RAPIDStrand, as isotope selection may play an important role. The same is true of D90, V150 prostate, and V150 urethra.

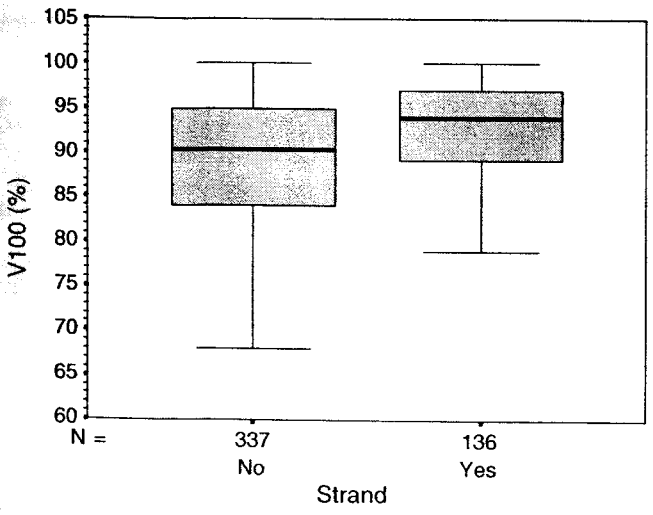

Fig. 1. Boxplot of V100 by strand vs. no strand.

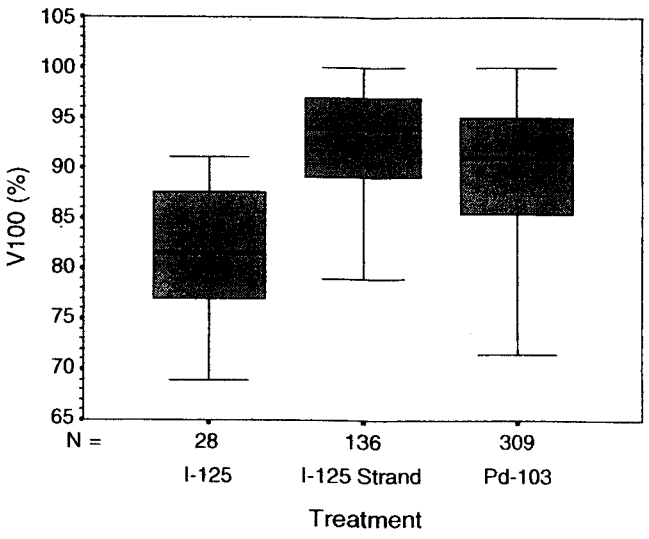

Fig. 2. Boxplot of V100 by isotope and strand.

Table 3
Best fit linear regression for V100

	P	Effect size[1]
^{100}Pd vs. ^{125}I	<0.005	0.08
Primary vs. boost	<0.005	0.03
RAPID Strand vs. loose	<0.005	0.12
Hormone treatment	0.4	n/a
Pre-implant prostate volume	0.9	n/a
Age	0.5	n/a

[1] Partial η^2.

where significant differences were also noted (Table 2). These data support the notion of improved dose homogeneity within the prostate gland with RAPIDStrand over free seed techniques, although isotope selection cannot be ruled out as a determinant.

Other authors have compared ^{103}Pd versus ^{125}I (14, 31). Even though it has been theorized that ^{103}Pd might be a better choice for high-grade lesions and ^{125}I for lower grade ones, Wallner *et al.* (31) and Cha *et al.* (14) observed similar biochemical control rates for the two isotopes. Fuller and Koziol (32) evaluated several factors using V100 as an indicator of implant quality. They found stranded source type and ^{125}I to be significant predictors of a higher V100, resulting in a better implant.

An additional factor not well described in the literature is the use of extra seeds used to fill in "cold spots" at the completion of the implant. In the loose seed era, we customarily used extra seeds in about 10–15% of the cases based on cold spots on fluoroscopy due to intraprostatic seed migration as well as peripheral seeds migrating away from the prostate gland. In the RAPIDStrand era, it is unusual for us to use added seeds since we have rarely observed seed migration within or outside the prostate (less than 2%).

It is possible that a "learning curve" contributed to the differences in outcome, especially with reference to free ^{125}I, as improved outcomes mirrored the temporal sequence of free ^{125}I, free ^{103}Pd, and RAPIDStrand ^{125}I techniques.

In summary, using V100 as an indicator of implant quality for our patients, this RAPIDStrand approach demonstrates an advantage over the standard, free-seed method previously used. This technique has also been associated with a lower urinary retention rate, although isotope selection may also play an important role.

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RADIOACTIVE SEED MIGRATION TO THE CHEST AFTER TRANSPERINEAL INTERSTITIAL PROSTATE BRACHYTHERAPY: EXTRAPROSTATIC SEED PLACEMENT CORRELATES WITH MIGRATION

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CLINICAL INVESTIGATION **Prostate**

RADIOACTIVE SEED MIGRATION TO THE CHEST AFTER TRANSPERINEAL INTERSTITIAL PROSTATE BRACHYTHERAPY: EXTRAPROSTATIC SEED PLACEMENT CORRELATES WITH MIGRATION

JEFFREY S. ESHLEMAN, M.D.,* BRIAN J. DAVIS, M.D., PH.D.,* THOMAS M. PISANSKY, M.D.,* TORRENCE M. WILSON, M.D.,† MICHAEL G. HADDOCK, M.D.,* BERNARD F. KING, M.D.,‡ CHARLES H. DARBY, M.S.,§ WAYNE N. LAJOIE, B.S.,* AND ANN L. OBERG, PH.D.§

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Purpose: To examine the incidence of seed migration detected on chest X-ray and to identify the predictors associated with its occurrence.

Methods and Materials: Between May 1998 and April 2000, 102 patients underwent permanent prostate brachytherapy at our institution and 100 were eligible for the study. Chest X-rays obtained at follow-up were examined for the number and location of seeds. The patient and treatment variables potentially associated with the occurrence and number of seed migrations were analyzed.

Results: One or more seeds were identified on the chest X-rays of 55 (55%) of 100 patients. The mean number of intrathoracic seeds in patients with migration was 2.2 (range, 1–10), and the proportion of seeds that migrated to the thorax was 0.98%. The rate of extraprostatic seeds planned was 43.9%, and postimplant CT identified 37.9% in such a location. The number of seeds planned for extraprostatic placement and below the apex were statistically significant ($\alpha = 0.05$) predictors in univariate logistic analysis. Multivariate analysis revealed the planned number of extraprostatic seeds as the only statistically significant predictor ($p = 0.04$).

Conclusion: Extraprostatic placement of loose seeds is associated with an increased likelihood for, and frequency of, seed migration to the thorax. Nonetheless, the small proportion of implanted seeds that migrated (≤1%) is highly unlikely to have significant dosimetric consequences. © 2004 Elsevier Inc.

Brachytherapy, ^{125}I, Migration, Prostatic neoplasms, Radiotherapy.

INTRODUCTION

In 2003, an estimated 220,900 men in the United States were diagnosed with adenocarcinoma of the prostate and 28,900 men died of this cancer (1). With the advent of prostate-specific antigen screening, most prostate cancer diagnoses are made in the early stages. An increasingly used option in the management of early-stage prostate cancer is transperineal interstitial permanent prostate brachytherapy (TIPPB) (2).

A unique property of TIPPB is the possibility of radioactive seed migration. In 1988, Hempel *et al.* (3) reported on a patient who underwent ^{125}I interstitial therapy for carcinoma of the anus and was later found to have metallic seeds on chest X-ray (3). Subsequently, Steinfeld *et al.* (4) reported chest migration of a radioactive seed after TIPPB. Gupta *et al.* (5) later reported seed migration to the chest from various anatomic sites after interstitial brachytherapy. In recent years, the increased use of TIPPB has led to multiple reports of radioactive seed migration to the chest (4, 6–13). Published rates, as summarized in Table 1, range from 0.6% to 29% of patients with one or more seeds found on a postimplant chest X-ray (CXR). Published patient and treatment parameters influencing the incidence and rate of seed migration include the use of Vicryl sutures, number of seeds implanted, planning volume, and number of loose seeds placed (7, 10).

The basis of radioactive seed migration seems clear; the prostatic capsule has a rich venous plexus with vessels large enough to accommodate seeds. Seeds placed extraprostatically have access to this plexus and often migrate away from their intended position via access to the venous circulation. Through the venous pathway, seeds migrate through the inferior vena cava, right chambers of the heart and into the pulmonary circulation. Because of their size and rigid-

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Table 1. Chest migration in reported TIPPB series

Study	Isotope	Patients with seed migration to chest (%)	Rate of seed migration to chest (%)	Maximum seeds to migrate in 1 patient (*n*)
Present study	^{125}I and ^{103}Pd	55.0% (55/100)	0.98% (119/12,135)	10
Grimm *et al.* (12)	^{125}I and ^{103}Pd	17.6% (39/221)	Not reported	3
Merrick *et al.* (7)	^{125}I (Rapid STRAND in periphery)	21.4% (18/84)	0.18% (24/13,467)	Not reported
	^{103}Pd	22.2% (16/72)	0.28% (29/10,338)	Not reported
	Overall	21.8% (34/156)	0.22% (53/23,805)	Not reported
Nag (8)	^{103}Pd	17.8% (19/107)	0.30% (32/10,612)	2
Older (13)	^{103}Pd	29.0% (32/110)	Not reported	4
Steinfeld *et al.* (4)	^{125}I	20.0% (1/5)	0.80% (5/600)	5
Tapen *et al.* (10)	^{125}I (Rapid STRAND in periphery)	0.7% (1/143)	Not reported	2
	^{125}I loose	10.0% (1/10)	Not reported	Not reported
	^{103}Pd	11.0% (15/126)	Not reported	Not reported
	Overall	5.9% (17/289)	Not reported	Not reported

Abbreviation: TIPPB = transperineal interstitial permanent prostate brachytherapy.

ity, seeds lodge in the end arterioles of the pulmonary system where, owing to their metallic content, they can be easily visualized by CXR.

To date, no untoward clinical consequences have been reported when pulmonary embolization has occurred (4, 6–13). However, it is conceivable that seeds could migrate or become entrapped in other organ systems. In this regard, autopsy-documented evidence has recently been published of seeds lodged in the right ventricle of the heart (14) and in a coronary artery as visualized by angiography (15).

Other potential consequences of seed migration include dosimetric consequences (16). Seeds lost to migration detract from the overall dose meant to cover the planning target volume. Merrick *et al.* (7) reported that pulmonary seed embolization accounted for only 10% of the seeds absent after orthogonal films were taken of the pelvis after implantation. Thus, CXR detection alone may significantly under represent the total seed loss from the target volume.

Migration rates have been linked to technical differences in TIPPB, which have been previously reviewed (17). Many institutions perform a modified peripheral loading technique in which loose seeds are placed. Most seeds are placed in the periphery of the gland to administer a homogenous dose and limit severe overdosing to the urethra. A typical margin of 3–5 mm is planned around the prostate (18) to account for extraprostatic tumor extension (19, 20), the accuracy of delivering the radiation dose to the target volume (21, 22), and the accuracy of the imaging technology used in the procedure. Other factors influencing migration rates may include both patient and tumor characteristics. The purpose of this study was to examine both clinical and treatment-related factors associated with migration of seeds to the thorax.

METHODS AND MATERIALS

Patient characteristics

The patient characteristics are given in Table 2. Between May 1998 and April 2000, 102 patients with Stage T1-T2 prostate cancer underwent TIPPB at our institution of whom 100 were included in this study. All patients underwent transrectal ultrasound (TRUS)-based planning using a modified peripheral loading technique and loose seed placement. Post-TIPPB dosimetry was evaluated by CT within 30 days after the date of the procedure. PA and lateral CXRs obtained at follow-up were examined for the number and location of seeds. Patient and treatment variables potentially associated with the occurrence and number of seed migrations were analyzed.

Preimplant planning

All patients underwent TRUS-based preplanning using the Theraplan Plus 3.0 system (Theratronics, MDS Inc., Toronto, Ontario, Canada). The planning target volume was created by placing a 3–5-mm margin around the prostate, except in the posterior and superior directions. Posteriorly, in proximity to the rectum, and superior to the bladder base, a smaller margin was used.

TIPPB procedure and postimplant CT scanning

The TIPPB procedure has been previously described (23); it includes the use of a Mick applicator and a modified peripheral loading technique. Ninety-seven patients underwent ^{125}I implantation and three underwent ^{103}Pd implantation. Ninety-nine patients were treated with TIPPB as monotherapy, and one received combination external beam radiotherapy and TIPPB. All patients were admitted postoperatively to the hospital overnight, and a Foley catheter was placed in each. Urine and Foley catheter bags were inspected and surveyed for displaced seeds. Patients rou-

Table 2. Patient and treatment characteristics

Characteristic	Patients (*n*)	Mean (range)
Age (y)		68.8 55–70
Tumor stage (1997 AJCC)		
T1c	63 (63)	
T2a	35 (35)	
T2b	2 (2)	
Pretreatment PSA (ng/mL)		6.3 0.7–16.3
PSA (ng/mL)		
0.0–4.0	24 (24)	
4.1–10.0	64 (64)	
>10.0	12 (12)	
Gleason score		6 (4–7)
4–5	15 (15)	
6–7	85 (85)	
Pretreatment ultrasound volume (cm^3)		43.3 (16–98)
Postimplant CT volume (cm^3)		56.7 (20–124)
Time to postimplant CT (days)		5.7 (0–57)
Radioisotope (Gy)		
^{125}I	97 (97)	
^{103}Pd	3 (3)	
Seeds planned (*n*)		113.1 (58–192)
Seeds placed (*n*)		123.8 (60–214)
Needles implanted (n)		30.3 (18–50)
mCi per source (^{125}I only)		0.4 (0.3–0.5)
Total mCi implanted (^{125}I only)		48.1 (22.2–82.2)

Abbreviations: AJCC = American Joint Committee on Cancer; PSA = prostate-specific antigen.

Data in parentheses are percentages, unless otherwise noted.

tinely underwent postimplant CT scanning within 2 days after their procedure. The prostate was contoured on the CT image by the treating radiation oncologist. Postimplant dosimetric analysis was performed according the American Brachytherapy Society recommendations (24).

Statistical analysis

The preplans were reviewed and the following information was recorded: preimplant prostate size in cubic centimeters as determined by TRUS planimetry and prolate spheroid calculation, number of needles planned, total number of seeds planned and placed, and postimplant prostate size in cubic centimeters by CT contouring. Preplanning ultrasonography and postimplant CT were then carefully reviewed for peripheral and extraprostatic seed placement. Extraprostatic seed placement was defined as any digitally reconstructed seed falling completely outside the CT-contoured prostatic capsule or planimetric margin. Peripheral seed placement was defined as any extraprostatic seed or any digitally reconstructed seed falling on the CT-contoured prostatic capsule or margin. Seeds planned and placed above the base and below the apex were analyzed separately as well as included in the extraprostatic group. An example of a preplan TRUS image identifying extraprostatic and peripherally labeled digitally reconstructed seeds is shown in Fig. 1.

All patients whose records were used in this analysis had previously provided consent for use of their records in retrospective medical research. Univariate analyses were prepared and examined to ascertain any transformations that would be necessary before subsequent model building ensued. Predictors were transformed using the natural logarithm function to reduce skewness of distribution if appropriate. Univariate and multivariate logistic models of occurrence of seed migrations were performed.

RESULTS

Of the 102 patients whose medical records were considered for use in this study, 1 did not have a postoperative CXR and 1 refused research authorization. Thus, 100 patients with one or more postimplant CXR were evaluated. One or more seeds were identified on the CXRs of 55 (55%) of 100 patients. A total of 119 (0.98%) of 12,135 seeds implanted were identified on CXR. The mean number of intrathoracic seeds in patients with migration was 2.2 (median, 2; range, 1–10). The distribution of seeds on CXR (Table 3) was 11 right upper lobe, 3 right middle lobe, 74 right lower lobe, 3 left upper lobe, and 26 left lower lobe and 2 autopsy proven seeds in the right cardiac ventricle. The proportion of extraprostatic seeds planned was 43.9%, and 37.9% were actually placed in an extraprostatic location as ascertained by postoperative CT imaging (Table 4). The number of seeds planned for extraprostatic placement and inferior to the apex was a statistically significant predictor of seed migration in univariate logistic analyses at the $\alpha = 0.05$ level (Table 5).

Three additional predictors were suggestive of significance at or below $\alpha = 0.14$. These included the number of seeds planned for implantation above the prostate base, number of peripheral seeds for implantation, and natural log of time from the procedure to the first CXR. All five predictors were tested in multiple logistic models via a stepwise model building process. *A priori,*, a four-predictor model was also considered on the basis of our knowledge. The predictors considered were the number of seeds planned for implantation at the prostate periphery and below the apex, the total number of seeds planned for placement, and the interval (expressed as natural logarithm [LnT]) from TIPPB until the first CXR. Subsequent evaluation indicated that the multiple predictor models were unstable and provided no usable information. Consequently, multivariate analysis revealed the planned number of extraprostatic seeds as the only statistically significant predictor ($p = 0.04$). LnT was suggestive of an effect ($p = 0.053$).

No toxicity was reported from chest migration of the radioactive seeds. Although the patient with two ^{125}I seeds found within the right ventricle died of a cardiac event, he had had a long history of heart disease, and the cause of death was not attributed to the embedded seeds (14).

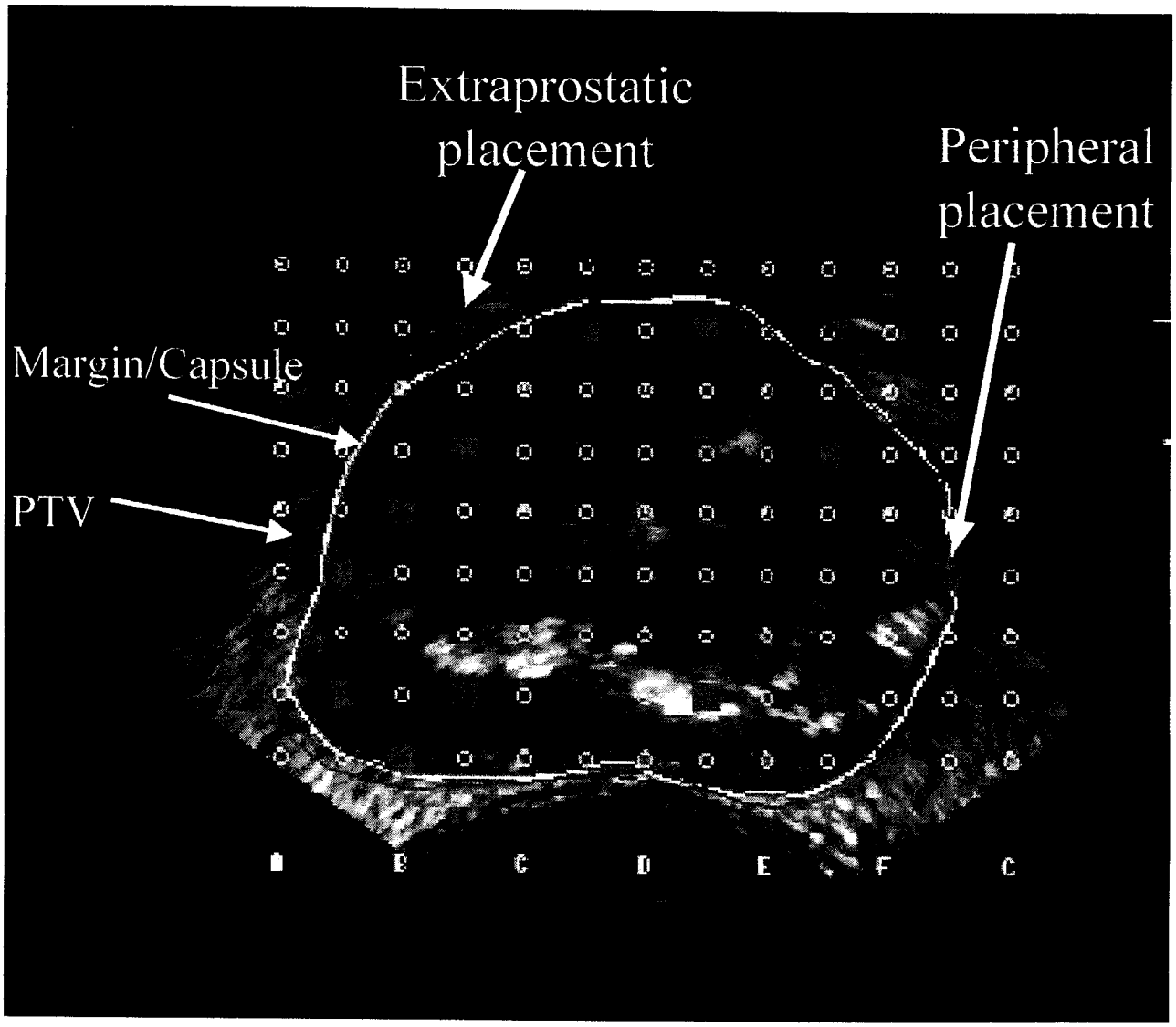

Fig. 1. Preimplant planning ultrasound scan. Extraprostatic seed placement defined as any digitally reconstructed seed falling completely outside contoured prostatic capsule or margin on ultrasound imaging. Peripheral seed placement defined as any extraprostatic seed plus any digitally reconstructed seed falling on contoured prostatic capsule or margin on ultrasound imaging. Similar method also applied to evaluation of postimplant CT scans.

Table 3. Seed migration to chest

Lobe of lung	Patients (*n*)	Total seeds migrating to chest (%)	Range
RUL	7	11/119 (9)	1.0–3.0
RML	2	3/119 (3)	1.0–2.0
RLL	41	74/119 (63)	1.0–8.0
LUL	3	3/119 (3)	1.0–2.0
LLL	19	26/119 (22)	1.0–2.0
Heart*	1	2/119 (2)	—

Abbreviations: RUL = right upper lobe; RML = right medial lobe; RLL = right lower lobe; LUL = left upper lobe; LLL = left lower lobe.

* Autopsy proven.

DISCUSSION

We report the postimplant seed migration rate to the chest in 100 of the first 102 consecutive patients undergoing TIPPB at our institution. Fifty-five percent of the 100 patients had seed migration to the chest after TIPPB. As summarized in Table 1, this rate was greater than in any previous study on seed migration. However, the total number of seeds found on CXR accounted for <1% of seeds implanted into the prostate and periprostatic tissue. This latter finding is consistent with that of other studies pertaining to the use of loose seeds. The results of the present study differ from many others in that the percentage of seeds planned for extraprostatic placement exhibited a high correlation with seed migration. It also differs in that a thorough review of both PA and lateral CXRs before and after TIPPB was performed.

Table 4. Peripheral and extraprostatic seed placement by pre- and postimplant imaging

Seed placement	Planned preimplant TRUS	Actual postimplant CT
Average proportion of extraprostatically placed seeds	39% (43.9/113.1)	31% (37.9/123.8)
Average proportion of peripherally placed seeds	60% (68.3/113.1)	47% (58.6/123.8)
Average proportion of seeds placed inferior to the apex	7% (8/113.1)	4% (4.7/123.8)
Average proportion of seeds placed superior to the base	6% (7/113.1)	3% (3.6/123.8)

Abbreviation: TRUS = transrectal ultrasonography.

The high rate of seed migration found in this report may be attributed to several factors. First, CXRs were available for review in >98% of the 100 study patients. This patient evaluation rate contrasts with several other studies such as that of Older (13) in which only 110 (60%) of 183 patients had postimplant CXRs available for review. Whether the 60% of patients was representative of the group as a whole was not indicated, so the overall seed migration rate in their patients may have been different. In the present study, preoperative CXRs were available for comparison allowing selective identification of migrated seeds even in the presence of multiple surgical clips in the chest from prior coronary artery bypass grafts or other surgical interventions. The identification of seeds from CXRs showing multiple surgical clips in patients with prior chest surgery without pre-TIPPB CXRs for comparison may add a source of uncertainty. From a review of plain film imaging, it is clear that diagnostic-quality PA and lateral CXRs more thoroughly and readily identify seeds than would a limited PA view on a fluoroscopic simulator. Some patients had seeds near the diaphragm, which were only identifiable as such on a lateral CXR. Finally, the results of our study suggest that the timing of the CXR may be relevant to the occurrence of seed migration. The greater the duration between TIPPB and subsequent CXR, the more likely that seed migration might be detected. In our series, CXRs were usually obtained 2–3 months after TIPPB; CXRs were obtained much sooner after the procedure in some other reports. This observation is consistent with that of Merrick *et al.* (7) who observed an increasing rate of seed migration depending on the timing of post-TIPPB CXR.

Table 5. Univariate analysis of patient and treatment parameters with seed migration to chest

Parameter	*p*
Total seeds planned for extraprostatic placement (TRUS)	0.03
Total seeds planned for placement inferior to the apex (TRUS)	0.03
Total seeds planned for peripheral placement (TRUS)	0.06
Time from implant to CXR	0.14
Total seeds planned for placement superior to base (TRUS)	0.21
Total number of seeds planned	0.35
Total number of seeds placed	0.36
Radiation oncologist	0.38
Seeds placed peripherally (postimplant CT)	0.45
Seeds placed extraprostatically (postimplant CT)	0.55
Seeds placed inferior to apex (postimplant CT)	0.60
Postimplant CT volume	0.63
Pretreatment TRUS volume	0.86
Actual seeds placed superior to base (by postimplant CT)	0.92

Abbreviations: TRUS = transrectal ultrasonography; CXR = chest X-ray.

TRUS used for preplanning; CT used for postimplant imaging and dosimetry analysis.

In the present study, regression analysis revealed that extraprostatic seed placement in the TRUS preplan correlated with migration. This finding is consistent with observations made during TIPPB in which seed migration was witnessed by fluoroscopy, particularly as seeds were placed anterior to the prostate where abundant venous drainage exists (25). The anterior and lateral periprostatic locations appear more prone to seed migration than other periprostatic locations. Nonetheless, seed migration has also been observed with intraprostatic seed placement, albeit much less frequently than with extraprostatic placement. No other study, to our knowledge, has confirmed the clinical observation that extraprostatic seed placement as per TRUS preplanning correlates with migration. Treatment of extraprostatic extension of prostate cancer is accomplished using a 3–5-mm dosimetric margin (19, 20, 26). TIPPB may treat extraprostatic extension with placement of a portion of the seeds in extraprostatic locations (27). In a survey report on experienced brachytherapists by Prete *et al.* (28), 53% of respondents reported using a 5-mm treatment margin. On the basis of this response and radiation dosimetric considerations, it is likely that the placement of some seeds in extraprostatic locations remains a common and arguably rational approach to TIPPB (27). In a related study by Butzbach *et al.* (29), examination of treatment margins and seed placement was conducted. Seeds were implanted in extraprostatic locations only at the prostatic base and apex, and the treatment margins were judged adequate to treat extraprostatic extension by postimplant CT-based dosimetric analysis. Nonetheless, and in principle, it appears possible that a dosimetric margin may be achieved if intraprostatic peripheral seed location is within 1–2 mm of the prostatic capsule or edge. Intraprostatic seed placement, without extraprostatic placement, would then likely result in lower rates of seed migration. Technical factors, including prostate mobility, seed tracking at implantation, degradation of the TRUS image, and operator error limit such precise

placement of all seeds. In a study by Yu *et al.* (30), it was noted that seed placement may occasionally vary by up to 1 cm from the intended position. In a related study (21), supplemental implantation in a prostate phantom on a "mock" cold implant was examined. Seed placement accuracy under idealized conditions with an experienced practitioner using a Mick applicator was determined. Seed placement accuracy as determined by all 41 supplemental seeds implanted ranged from 0 to 7.5 mm (mean ± standard deviation 2.3 ± 2.3 mm). Roberson *et al.* (22) found similar source placement error, with an average displacement of 4.6 mm. Such findings suggest that exclusive intraprostatic seed placement may not approach the accuracy desired to ensure complete treatment of a 3–5-mm periprostatic margin and planning target volume.

Evaluation of the preimplant TRUS-based plans revealed a rate of planned extraprostatic seed placement of 39% and an observed rate of placement of 31% by postimplant CT. Another seed placement definition, termed "peripherally placed," incorporates those seeds that are on the "line" of the contoured prostate, in addition to the seeds placed in extraprostatic locations. This latter definition is meant to account for seeds that are at the prostatic margin and may be more prone to migration than just those that are placed in extraprostatic locations. Furthermore, this definition accounts for the uncertainty in prostate segmentation whereby seeds judged to be at the prostate margin are actually in extraprostatic locations. To our knowledge, no other study, other than that of Merrick *et al.* (7), has reported either of these values, but comparisons between studies might be difficult because of the known rates of interobserver and intraobserver variability in post-TIPPB prostate contouring (31). Nevertheless, Merrick *et al.* (7) reported a rate of 41.3% extraprostatic seed placement, comparable to the rate of 39% reported in our study. Their study did not, however, find a correlation with extraprostatic seed placement and embolization; otherwise, their findings are consistent with many of those described in the present study.

It is remarkable that the planned extraprostatic placement of seeds as determined by preimplant TRUS correlated with seed migration and extraprostatic seed placement as determined by postimplant CT scanning did not. This finding may be attributable to differences in reproducibility and variability of preimplant TRUS and post-TIPPB CT imaging in segmentation of the prostate such that the preplan more accurately reflects extraprostatic seed placement. Although no recent studies directly comparing the reproducibility of preimplant TRUS with postimplant CT have been published, several studies have demonstrated that observer variability in postimplant CT segmentation is significant. In a study by Dubois *et al.* (31), interobserver and intraobserver variabilities of postimplant CT and MRI were measured and revealed that a difference of 5 mm routinely occurs in establishing prostate dimensions. Lee *et al.* (32) and Al-Qaisieh *et al.* (33) have reported that interobserver variability in postimplant prostate segmentation on CT images resulted in differences that were statistically significant with respect to predicted dosimetry. In detailed studies by Narayana *et al.* (34, 35), difficulties and differences in registering TRUS and CT for treatment planning related to TIPPB were evident. In contrast, Sech *et al.* (36) have demonstrated relatively good interexaminer reliability of TRUS prostate volume estimation using a prolate ellipsoid calculation. Furthermore, Tong *et al.* (37) have shown that step-section TRUS planimetry similar to that used in TIPPB planning has less variability in prostate volume determination than the ellipsoid method.

Patients at our institution are counseled before TIPPB that seed migration to the chest and other locations may occur. Although no untoward effects from seed migration have been observed, reducing the rate of migration after TIPPB nonetheless seems an intrinsically worthwhile endeavor. One method of reducing seed embolization is to use seeds that are packaged in absorbable suture material (10). Tapen *et al.* studied 289 consecutive patients who underwent TIPPB with the use of sutured seeds (n = 143) placed at the periphery or with loose seeds only (n = 146). The rate of seed migration in those patients with sutured seeds was 0.7% and for those with loose seeds was 11%. In their study, the postimplant CXRs were performed on the day after the procedure, so that the rate of longer term seed migration from sutured seeds may have been greater, as has been noted by Merrick *et al.* (7). Nonetheless, Tapen *et al.* (10) demonstrated a clear advantage in reducing seed migration with use of seeds in absorbable suture material. A delay in the timing of seed migration, if it is to occur, may have favorable dosimetric consequences compared with immediate seed migration. Similarly, Merrick *et al.* (7) found that the proportion of Vicryl suture-encapsulated seeds implanted influenced the rate of seed migration. Histopathologic examination of salvage prostatectomies after TIPPB failure has demonstrated that a fibrous capsule may form around the seeds after a period (14). Such observations are consistent with those described in reports on radiation pathology (38) and provide an explanation for the relative "fixity" of seeds embedded in Vicryl suture material after the suture material has been absorbed. The use of seeds in Vicryl suture material may, therefore, be considered if significant extraprostatic seed placement is contemplated in the planning process, because its use may reduce seed migration.

CONCLUSION

The number of loose seeds placed in extraprostatic locations as per the TRUS preplan correlated with an increased likelihood of seed migration to the thorax. This finding is consistent with observations made with fluoroscopy during TIPPB. Although a substantial proportion of patients had seed migration to the thorax, the small proportion of implanted seeds that migrated (≤1%) is not likely to have adverse dosimetric or patient health consequences. Until the dosimetric affects of peripheral seed loss are quantified, attention to the proportion of seeds planned for extraprostatic placement appears warranted when using a free seed approach.

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~~CMS-4125-P-3~~

Medicare Program; Reporting Hospital Quality Data for FY 2008 Inpatient Prospective Payment System Annual Payment Update Program HCAHPS Survey, Surgical Care Improvement Project (SCIP), and Mortality

Submitter : Mr. Dan Rode **Date & Time:** 10/05/2006

Organization : American Health Information Management Association

Category : Other Health Care Professional

Issue Areas/Comments

GENERAL

GENERAL

See Attachment

CMS-4125-P-3-Attach-1.DOC

AHIMA #
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October 5, 2006

Mark McClellan, MD, PhD
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-1506-P
PO Box 8011
Baltimore, Maryland 21244-1850

Re: File Code CMS-1506-P
File Code CMS-4125-P

Medicare Program; Changes to the Hospital Outpatient Prospective Payment System and Calendar Year 2007 Payment Rates; Proposed Rule (71 *Federal Register* 49506)

Dear Dr. McClellan:

The American Health Information Management Association (AHIMA) welcomes the opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS') proposed changes to the Hospital Outpatient Prospective Payment System (OPPS) and calendar year 2007 Rates, as published in the August 23, 2006 *Federal Register*. Our comments focus on those areas of particular interest to our members.

AHIMA is a not-for-profit professional association representing more than 50,000 health information management (HIM) professionals who work throughout the healthcare industry. AHIMA's HIM professionals are educated, trained, and certified to serve the healthcare industry and the public by managing, analyzing, reporting, and utilizing data vital for patient care, while making it accessible to healthcare providers and appropriate researchers when it is needed most.

Consistency in medical coding and the use of medical coding standards in the US is a key issue for AHIMA. As part of this effort, AHIMA is one of the Cooperating Parties, along with CMS, the Department of Health and Human Services' (HHS) National Center for Health Statistics (NCHS), and the American Hospital Association (AHA). The Cooperating Parties oversee correct coding rules associated with the *International Classification of Diseases Ninth Revision, Clinical Modification* (ICD-9-CM).

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AHIMA participates in a variety of coding usage and standardization activities in the US and internationally, including the American Medical Association's (AMA's) Current Procedural Terminology® (CPT®) Editorial Panel.

AHIMA and its members also participate in a variety of projects with other industry groups and agencies of the Health and Human Services Department related to the use of secondary data for a variety of purposes including quality monitoring, reimbursement, public health, patient safety, biosurveillance, and research.

VIII-B: Proposed CY 2007 Drug Administration Coding Changes (71FR49600)

Currently, a combination of CPT and HCPCS level II codes are required by Medicare for facility reporting of drug administration services. Many private payers require the reporting of only CPT codes, resulting in a situation whereby hospitals are required to use different coding schemes to report drug administration services to different payers. Dual coding systems for drug administration services is administratively burdensome for hospitals and also results in data incomparability.

While we recognize that the CPT codes for drug administration services were designed for physician reporting purposes and have been somewhat confusing and difficult to apply in the facility setting, we do not believe that creation of a separate set of codes for Medicare use is a satisfactory solution, since many other payers require the use of the full set of CPT codes for drug administration services.

Consistent coding practices across payers would be less administratively burdensome and would result in improved data accuracy and comparability. We also believe that the HIPAA regulations for electronic transactions and code sets were intended to ensure that multiple code sets wouldn't be used to report the same service.

AHIMA recommends that CMS adopt the full set of CPT drug administration codes for use under the OPPS. Hospitals are already using the full set of CPT codes for reporting to many non-Medicare payers. Currently, however, the CPT codes are not intuitive and easily applicable to the hospital setting. Clarification of definitions, code descriptions, and instructions is necessary in order for hospitals to be able to report these codes accurately and consistently. CMS should work with AHIMA, the American Hospital Association and the American Medical Association to provide additional guidance to hospitals on the proper use of these codes for facility reporting, including instructions for the application of the terms "initial," "subsequent," "sequential," and "concurrent." If necessary, CMS should also work with these three organizations to develop proposed CPT code modifications to address specific issues pertaining to facility reporting of drug administration services.

IX: Proposed Hospital Coding and Payment for Visits (71FR49604)

We appreciate CMS' consideration of the facility visit coding guidelines developed by the American Hospital Association (AHA)/AHIMA Expert Panel and posting these guidelines for wider

public input. We also appreciate CMS' acknowledgement that the AHA/AHIMA guidelines are the most appropriate and well-developed guidelines for use in the OPPS. AHIMA looks forward to working with AHA and the Expert Panel to refine the guidelines to address concerns and suggestions raised by CMS and the public. We support CMS' commitment to provide a minimum of 6 to 12 months notice to hospitals prior to implementation of national guidelines. This timeframe will allow adequate education of hospital staff on the proper application of these guidelines and the documentation requirements necessary to support code levels.

We note that the AHA/AHIMA guidelines were submitted to CMS over three years ago, and some of the specific revisions CMS chose to make in their modified version, as well as other suggestions for modifications, could be a reflection of changes in clinical practice since the AHA/AHIMA guidelines were originally developed. If these guidelines had been implemented soon after their development, undoubtedly refinements would have been made since then.

CY 2007 Proposed Coding: **AHIMA opposes the creation of new G-codes to replace hospitals' reporting of the CPT emergency department and clinic evaluation and management (E/M) codes for CY 2007.** We believe that CMS should not implement new codes in the absence of accompanying national code definitions and national guidelines for their application. The CPT E/M codes should continue to be used until national guidelines are ready for implementation. Creating new codes without a set of national guidelines will increase confusion and add a new administrative burden requiring hospitals to manage two sets of codes – the proposed G-codes for Medicare and CPT E/M codes for non-Medicare payers – without the benefit of a standardized methodology or improved data.

Even when national guidelines are developed, AHIMA does not believe that temporary G-codes should be created for facility visit coding. A formal proposal should be presented to the American Medical Association's CPT Editorial Panel to create CPT codes for hospital emergency department and clinic visits. These codes could then be used by all payers. New codes and the accompanying national guidelines should not be implemented until CPT codes have been implemented.

CMS' Contracted Study to Validate AHA/AHIMA guidelines: In response to concerns raised by CMS' contracted study of the AHA/AHIMA guidelines, we would like to point out that these guidelines were never intended to be used as a stand-alone document without additional explanation and educational materials. We expected to develop supplemental materials, in conjunction with AHA, to clarify proper application of the guidelines after they were adopted by CMS for implementation under the OPPS. Therefore, in the absence of this additional guidance, it is not surprising that the contractor identified elements in the guidelines that were difficult to interpret or poorly defined. Also, it is not clear, by CMS' own admission, whether the contractor had access to the complete medical records.

CMS noted that they were unable to draw conclusions about the relationship between the distribution of current hospital reporting of visits using CPT E/M codes that are assigned according to each hospital's internal guidelines and the distribution of coding under the AHA/AHIMA guidelines. These findings reflect the fact that there is no set of national guidelines or a standard methodology for hospitals to develop their own guidelines. Through our participation on the AHA/AHIMA Expert Panel, we re-coded a sample of emergency department and clinic visit

records using several different hospitals' methodologies. This review revealed considerable variability in the levels of service reported, depending on which methodology was used.

Distinction Between Type A and Type B Emergency Departments: **AHIMA does not believe that the facility visit codes should distinguish between different types of emergency departments.** This is not a coding issue. The facility visit codes should be limited to describing the patient complexity and resource utilization. Other information, such as the type of emergency department where the visit occurred, should be captured through a separate methodology.

Other comments in response to CMS' concerns with the AHA/AHIMA guidelines can be found in a separate joint letter submitted by AHA and AHIMA as a result of our task force meetings.

XVIII-B-1-a: Proposed Revised ASC Payment System for Implementation January 1, 2008 – Proposed Definition of Surgical Procedure (71FR49636)

AHIMA supports the expansion of the definition of surgical procedure under the Ambulatory Surgical Center (ASC) payment system to include HCPCS level II and CPT category III codes which directly crosswalk to, or are clinically similar to, procedures in the CPT category I surgical range.

XX: Reporting Quality Data for Improved Quality and Costs Under the OPPS (71FR49665)

As AHIMA has noted in previous comments to CMS, we agree with the agency's desire to achieve a goal of value-based purchasing and promoting higher quality services. We acknowledge that taking the next step toward ambulatory care as offered by hospitals makes sense so long as it is recognized that eventually, sooner rather than later, any comparisons conducted on an ambulatory basis will have to cover non-hospital entities as well.

AHIMA is actively engaged in projects independently, with the Agency for Healthcare Research and Quality (AHRQ) and others to ensure that as standards for "performance data" and quality indicators are developed, implemented, and improved, the data and measures will be consistent and uniform geographically and across all sectors of the healthcare industry. We note CMS' comments on a "Hawthorne effect" coming from existing data and measure collection for hospitals. However, in the long run, it will be the ease of data collection, data uniformity, and trusted results that provide strong support for such data collection efforts. Consistency also permits those building the functional and data standards for the electronic health records to ensure appropriate secondary data is available for such purposes.

Everyone involved in the current efforts to develop an effective means for secondary data collection through paper records, the EHR, and hybrid environments, recognizes the difficulty of beginning and expanding the data collection efforts and the subsequent quality payment system that CMS and others are seeking. Until outpatient measures are developed and approved it appears acceptable in the short term to adapt the quality improvement mechanism provided by the IPPS (Reporting Hospital Quality Data for Annual Payment Update (RHQDAPU) and the proposed IPPS surgical

care improvement project (SCIP) measures. We are concerned, however, that adoption of the IPPS measures might delay work necessary for outpatient measures. CMS should work with the industry and other federal agencies to develop a strategic plan for outpatient measure standards. Input to this process needs time and must occur outside of a response to this NPRM. AHIMA's HIM professionals stand ready to work with CMS, AHR, HQA, AQA, NQF and others to ensure that appropriateness and consistency are developed across the outpatient sectors of the healthcare industry. As CMS has often noted, care rendered in hospital-based ambulatory needs to be compared to the same care that can be rendered in ambulatory surgical centers, physician offices, and other sites of service.

XXI: Promoting Effective Use of Health Information Technology (71FR49670)

AHIMA agrees that there is a mixed message regarding the potential of health information technology (HIT) to reduce costs. As alluded to in our comments on quality data reporting, we believe that is in the development, adoption, and implementation of standards that will lower costs and improve quality. Standards, consistency, and uniformity are necessary for software now, and as the industry moves forward in the implementation of a standard EHR and health information exchange (HIE); this includes standards for data, data definitions, terminologies, and classifications. The industry has started on the road toward President Bush's 2014 health information goal, however if we are to achieve this goal, the introduction of standards and requirements must take into account the paper to electronic transition currently under way and ensure that the development of secondary uses of data – like quality measurement – can be followed by organizations as they mature toward the EHR.

It is also important to note that with standards, quality measurement reporting or any secondary data reporting effort will be much easier, more accurate and much less costly once standard EHRs are in place. Before full use of EHRs is achieved collection of information in a paper or hybrid system remains a high consumer of human resources. The higher volume of outpatients as opposed to inpatients will also significantly inflate the costs and burdens of facilities, in as much as the same burden is often experienced with much lower reimbursement per encounter.

Development of a standard EHR and HIEs will not provide the full answer. Beyond the standardization of quality measures, for instance, CMS must take aggressive steps to ensure terminologies and classification standards are in place so that the quality or performance measurements can be evaluated with the condition of the patient. AHIMA urges the Health and Human Services Department (HHS) and the American Health Information Community (the Community), which include CMS, to adopt and provide for the implementation of modern terminologies such as those identified in the Consolidated Health Informatics (CHI), and especially the SNOMED-CT® adopted by CHI and approved by the National Committee on Vital and Health Statistics.

A standard EHR, with a SNOMED-CT terminology and functional standards and architecture designed to provide adequate and appropriate secondary data, will allow for achieving the goal of lowering costs and improving quality, but more is needed. The US must upgrade its primary

diagnoses classification system ICD-9-CM (volumes 1 and 2) to a 21st century standard ICD-10-CM.

The need for this change has been known for 13 years and the potential to resolve this need has been available since the turn of the century. But now, six years later, we have not moved to make the changes. Without the use of the ICD-10-CM classification, providers, health plans, QIOs, and others will continue to either rely on incomplete data coming from the claim, or demand additional data from providers – which translates into an inefficient use of resources and increased administrative costs for all.

It has been suggested that CMS finalize a rule for HIPAA attachments. AHIMA suggests instead that steps be taken to improve the initial data provided on the claims: the diagnosis and procedure codes. In addition, now that the industry has achieved electronic claims processing, AHIMA joins others and recommends that CMS and other payers accept and promote the transmission of all diagnostic and procedure codes associated with an encounter or stay, and not to limit this data (codes) to standards developed for paper claims in the 1980s (nine diagnoses on the UB-92).

XXII: Health Care Information Transparency Initiative (71FR49671)

While AHIMA supports the goal of transparency and the ability of healthcare consumers to have data on which to make choices, we must note that only through receiving and reviewing quality (appropriate, clear, consistent) information can a consumer make decisions to purchase quality healthcare. If data standards are not updated to reflect the contents of 21st century health records, and provide for consistent evaluation, the data provided to individuals is suspect. Much of the data used currently in quality measurement and payment comes from the claim. Yet the claim data is currently not capable of providing the detail necessary to accurately determine the diagnoses and procedures related to the patient's care. If transparency is the goal we must improve the data, not just the mechanisms to provide data.

XXIII: Additional Quality Measures and Procedures for Hospital Reporting of Quality Data for the FY 2008 IPPS Annual Payment Update (71FR49672)

Re: File Code CMS-4125-P

Most of AHIMA's comments on quality, above, also apply to this section. While we applaud CMS' further development of quality measures, we suggest they all be done in concert with the current AQA-HQA effort, and the recent recommendations of the Secretary for uniform measures across the industry. AHIMA is actively engaged in the goal of evaluating measures and highlighting gaps as well as working to ensure an appropriate standard EHR capable of producing secondary data that can support the uniform efforts and data collection mention here and above.

Since item 4 [71FR49674] relates to mortality, AHIMA must note that at some point CMS should consider the comparison of US mortality and morbidity data in its quest for quality measurement. Until ICD-10-CM and ICD-10-PCS are in use, such a comparison could be approached with a crosswalk between ICD-9-CM morbidity data, and ICD-10 mortality data. The additional

information contained in the US mortality database at the National Center for Health Statistics may prove most useful for full outcome information.

Conclusion

We appreciate the opportunity to comment on the proposed modifications to the Hospital OPPS. If AHIMA can provide any further information, or if there are any questions or concerns with regard to this letter and its recommendations, please contact Sue Bowman, RHIA, CCS, AHIMA's director of coding policy and compliance at (312) 233-1115 or sue.bowman@ahima.org, or myself at (202) 659-9440 or dan.rode@ahima.org.

Sincerely,

Dan Rode, MBA, FHFMA
Vice President, Policy and Government Relations

cc. Sue Bowman, RHIA, CCS

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BY FEDERAL EXPRESS

October 3, 2006

The Honorable Mark McClellan, MD
Department of Health and Human Services
Attention: CMS-1506-P
Mail Stop C4-26-05
7500 Security Boulevard,
Baltimore, MD 21244-1850.

RE: CMS-1506-P; Hospital Outpatient Prospective Payment System and CY2007 Payment Rates

Dear Dr. McClellan:

We have recently received a letter of denial for a New Technology APC code for the **Implantation of the DVS® Dosimeter**. As the Hospital Outpatient Prospective Payment System comment period for calendar year 2007 is currently in the proposed comment period, we would like to take this opportunity to submit the following remarks.

The original New Technology APC application was submitted May 26, 2005 for Implantation of the DVS Patient Dose Verification System. After final clearance was received from the FDA, an updated application was submitted May 3, 2006, for Implantation of the DVS Dosimeter which included additional FDA information pertinent to approval for this new technology.

CMS stated that the reason stated for denial of the code was that *"the service is described by existing HCPCS codes or combination of HCPCS codes".*

CMS's review of the product labeling found that the DVS System is to be "used for dose verification and not for adjustment of dose during treatment." This information lead CMS to conclude that, in the context of radiation treatment procedures, Implantation of the DVS Dosimeter is a part of quality assurance that is integrated into radiation oncology services provided to patients, and thus described by existing HCPCS code.

CMS has taken this particular section of the labeling out of context which has lead to a misunderstanding of the technology and the application. It is important to emphasize that the actual measurement of the radiation dose delivered to the targeted site and its subsequent interpretation was not part of our request for a New Technology APC code but rather the implantation of this new technology.

We have conducted a thorough review of the most recent product labeling and existing coding for radiation treatment procedures and would like to share with you some of our

findings. Before discussing the DVS technology in the context of its role in treatment planning and dosimetry, as opposed to quality assurance, it is important to review how and why this technology is different from existing dosimetry technologies. The application submitted was for the ***Implantation of the DVS Dosimeter***, which includes the DVS dosimeter.

The concept of an implantable dosimeter at the targeted site of radiation for the purpose of measuring the amount of radiation delivered meets all the CMS criteria as **new technology**. The DVS Dosimeter is the ***first and only implantable dosimeter*** of its kind making the technology, and its associated use, different and unique from existing technologies and procedures. As a result, the implantation of dosimeters is ***not*** described by existing codes, making the Implantation of the DVS Dosimeter eligible for a New Technology APC assignment.

Physicians will implant the DVS Dosimeter at the *start of therapy*, before the delivery of any radiation treatments. For this reason, *Implantation of the DVS Dosimeter* is an integral part of accurate treatment planning and dosimetry. Furthermore, the package labeling for the DVS states that "*DVS is specifically indicated for breast and prostate cancers to measure photon beam therapy and as an* adjunct to treatment planning *to permit measurement of the in vivo radiation dose received at the site of implant; for example, tumor periphery, tumor bed and/or surrounding normal tissues for validation of the prescribed dose.*" This labeling clearly states that use of the DVS, and hence its *implantation*, is part of the treatment planning process, and not part of quality assurance/treatment management.

The DVS, unlike any currently existing technology, provides critical information to providers that up to now, has been unavailable. Providers may have had the capability to verify dosage **settings** of treatment delivery devices compared to the prescribed dose, but they have never had the capability to measure the **actual radiation dose delivered in vivo** to the targeted site and compare the dose delivered to the prescribed dose. The DVS now makes this possible by placing the dosimeters at the targeted site of the radiation dose, as opposed to the skin surface, to insure the delivery of the prescribed tumoricidal dose of radiation.

Because this measurement is made from an *in vivo* source and in real time, it allows for absolute dosimetry, as opposed to a one time or periodic quality assurance check at the skin surface. Current dosimetry technology only permits dosimetry calculations from the skin surface. *In vivo*, absolute dosimetry, as determined by the DVS, provides the ability to identify dose errors not previously identified by quality assurance dosimetry such as inhomogeneity correction, tumor/organ shifting, tumor shrinkage and dose planning. DVS is also able to identify more common dose discrepancies related to patient setup and patient positioning. This is different from dosimetry for quality assurance. Dosimetry for quality assurance is most commonly used to identify initial set up errors at the surface only.

We would also like to take this opportunity to address the following package labeling:

> *"The DVS system is not intended to specify adjustments to dose. Dose measurement data obtained using the DVS System should be used in conjunction with existing planning and delivery tools to verify delivered dose rather than as a stand alone tool for determining dose adjustments".*

The first sentence of this statement was recommended specifically to discourage physicians from "chasing" or altering the measured dose variance from day to day. The FDA and Sicel Technologies agreed to make this wording more apparent by outlining it in a black box because both were concerned that physicians might use the daily difference between observed and expected dose, to raise or lower the subsequent day's dose. The concern was that using the information in this manner does not take into consideration the typical dose variation observed, and the fact that most cancer patients receive 25-30 radiation treatments, each with some variation in dose. This is not the intended use of the device. However, that said, the DVS ***is a part of the treatment planning process***. The second portion of the statement clearly positions use of the DVS in conjunction with treatment planning and delivery. Furthermore, specific guidelines following this statement, which were also approved by the FDA, include the following recommendations:

- Systematic dose deviations of ≥5-7% over a number of fractions should result in a re-evaluation of the treatment plan, patient setup, and equipment function to determine the reason for the variation. A change or correction to the plan should be considered after careful evaluation of the above mentioned parameters.
- Random variations of ≥5-7% observed in each of five or more consecutive measurements should result in an evaluation of positioning consistency or patient or organ movement during treatment.
- A single reading of 10% or greater should be immediately reported to the radiation oncologist and a review of the patient set up, treatment plan, and portal images should be undertaken.

Thus, although daily dose changes are to be avoided, ***changes to the treatment plan and dose adjustments or corrections are recommended***. The dosimeter's implantation before the start a radiation therapy, combined with aforementioned guidelines for use, clearly position the DVS as an adjunct to treatment planning and dosimetry.

We would like to thank you again for the opportunity to submit these comments. Should you have any additional questions, please do no hesitate to contact us.

Sincerely,
THE PINNACLE HEALTH GROUP, Inc.

Kathy Francisco, Principal
kfrancisco@thepinnaclehealthgroup.com

CC: Carol Bazell, MD, Acting Director, Division of Outpatient Care
Charles W. Scarantino, MD, PhD, Sicel Technologies, Inc.