

Comments

LCD Title

Proton Beam Therapy

Contractor's Determination Number

RAD-040

1. Comment

Three comments are related to the first paragraph in the policy.

a. In the section **Indications and Limitations of Coverage and/or Medical Necessity:**

In the last sentence of the first paragraph the sentence reads:

"In contrast conventional external beam radiation therapy (EBRT) delivers radiation to all involved tissue, diseased and normal, and targeted tissue receives 60-70% of the intended dose."

This is factually incorrect. I suggest replacement with the following:

"In contrast conventional external beam radiation therapy delivers radiation to a more broad range of diseased and normal tissues with the targeted tissue receiving approximately 100% of the intended dose but a larger volume of normal/unintended tissue receiving a significantly higher dose of radiation that is approximately 20-60% of the dose. In short there is a higher integral dose to the normal tissues with conventional external beam therapy."

b. In the first paragraph, under Indications and Limitations, is a statement that "conventional external beam radiation therapy (EBRT) delivers radiation to all involved tissue, diseased and normal and targeted tissue receives 60-70% of the intended dose."

This statement is incorrect. In conventional EBRT, the targeted tissue usually receives 95-100% of the intended dose. A major limitation of EBRT is that in some situations, because critical normal tissues cannot be completely protected from the radiation, a curative dose cannot be used.

c. In the first paragraph, under Indications and Limitations, is a statement that "conventional external beam radiation therapy (EBRT) delivers radiation to all involved tissue, diseased and normal and targeted tissue receives 60-70% of the intended dose."

This statement is incorrect. In conventional EBRT, the targeted tissue usually receives 95-100% of the intended dose. A major limitation of EBRT is that in some situations, because critical normal tissues cannot be completely protected from the radiation, a curative dose cannot be used.

Response

This entire section has been corrected and rewritten to reflect these changes.

2. Comment

I believe that the statement regarding the reduction in integral dose with protons at the end of the second paragraph is true but would benefit from expansion. The current statement is:

"Due to reduction in integral dose with protons the most important benefits can be expected/or pediatric patients."

I suggest changing this to say pediatric and younger patients. Certainly a patient who is 25 or 30 or perhaps even 40 would benefit similarly to the reductions in integral dose. Many second malignancies do take between 7 to 20 years to develop however patients in their early 20's and 30's would also be expected to benefit significantly. I would suggest adding this sentence following this amended sentence.

"They suffer the greatest risk from long term sequelae from these higher integral doses with conventional therapy."

Response

We have changed this section adding additional information.

3. Comment

Under the Group 1 headings #8 it is suggested that solid tumors in children up to 18. I would suggest changing this to in children up to age 18 and younger adults (S: 30 years old).

Response

We removed the age limit of 18.

4. Comment

I believe that there are several inconsistencies between Group 1 and Group 2. Most specifically in Group 1 head and neck malignancies are included but many of the diagnoses codes appropriate to head and neck cancer are not included in Group 1 but rather Group 2. This is both unclear and does not lead to a consistent policy.

Response

These inconsistencies have been rectified.

5. Comment

Two comments were received that lung cancer is listed in Group 1 but the diagnosis codes for these are lacking the Group 1 category. These are again unclear.

Response

Lung cancer has been moved to Group II along with the diagnosis codes

6. Comment

I believe the overall policy would benefit significantly from elimination of the Group 1 versus Group 2 category. I believe that the overall gist and intent is to create a system wherein the clear benefit of protons over conventional methods could be demonstrated. I would support a Group 1 categorization for all of the diagnoses listed with a clear statement that dose volume histogram evidence of benefit to critical normal structures must be demonstrated along with appropriate participation in a clinical trial or registry. We believe that this will contribute substantially to accruing data for necessary outcome studies. It will also demonstrate the clear dosimetric advantages that are potential with proton beam therapy. Both of these criteria should be met and if they are; there is really not a distinction between Group 1 and Group 2 elucidated in the current document hence merging appears to make the most sense. This is well illustrated in the policy of the Pennsylvania/Maryland etc region.

Response

We have decided to keep the two groupings for now hoping that as the literature arrives we can whittle down to one coverage group. We do not wish to discourage studies of Group I indications. We have expanded on the requirements as follows:

In addition to the criteria in Group I, Proton Beam Therapy indications must demonstrate that:

- The Dose Volume Histogram (DVH) one or more critical structures or organs protected by the use of Proton Beam Therapy;
- The dose to control or treat the tumor cannot be delivered without exceeding the tolerance of the normal tissue;
- There is documented clinical rationale that doses generally thought to be above the level otherwise attainable with other radiation methods might improve control rates; or
- There is documented clinical rationale that higher levels of precision associated with Proton Beam Therapy compared to other radiation treatments are clinically necessary.

For the treatment of primary lesions, the intent of treatment must be curative

- For the treatment of metastatic lesions, there must be
 - a. the expectation of a long-term benefit (Greater Than 2 Year of life expectancy) that could not have been attained with conventional therapy
 - b. the expectation of a complete eradication or improved duration of control of the metastatic lesion that could not have been safely accomplished with conventional therapy, as evidenced by a dosimetric advantage for proton beam radiotherapy over other forms of radiation therapy.
- The patient's record demonstrates why Proton beam radiotherapy is considered the treatment of choice for the individual patient. Specifically, the record must address the lower risk to normal tissue, the lower risk of disease recurrence, and the advantages of the treatment over IMRT or 3- dimensional conformal radiation. Dosimetric evidence of reduced normal tissue toxicity and/or improved tumor control must be maintained.

7. Comment

The paragraphs under Indications are confusing. The first statement is that proton beam therapy will be considered medically reasonable and necessary for the following conditions. These conditions are listed under Group I. The last paragraph following group I makes a statement "if the above provisions are met and the patient is treated in a protocol, etc." Does this mean that covered patients must be treated on a protocol, or that if they are treated on a protocol, it must be IRB approved?

Response

The policy now reads:

If the above provisions are met and the patient is treated in a protocol that is designed for evidence development and for future publication, it is expected that future published data will support an outcome advantage for Medicare patients for continued coverage of the specific diagnosis. The protocol in and by itself does not constitute criteria for coverage. The presence of an Institutional Review Board (IRB) review when appropriate and patient informed consent are also expected.

8. Comment

From the document, it appears that in patients with conditions listed under Group 2, proton therapy will be considered medically reasonable and necessary if the prior conditions are met and the patients are on a clinical trial.

Some of the Group 2 conditions overlap conditions listed in group 1: lesions of the paranasal sinuses could be considered head and neck cancer, cancers of the lung are listed in both groups.

Response

We have corrected these inconsistencies.

9. Comment

Several commentors requested that the WPS proposed DRAFT LCD for Proton Beam Therapy use Highmark Medicare Services LCD30314 as a model. This policy, from a jurisdiction that includes current proton treatment facilities, has a more clearly stated policy of medical necessity, and includes the full range of ICD-9 codes applicable to this treatment.

Response

We did use a combination of Highmark's and First Coast's policies to help form our first draft. The policy has subsequently been altered several times as a result of comments and information received.

10. Comment

In reference to Proton Beam Therapy, Indications should be limited to what is our current clinical experience. Also it should be limited to certain primary tumors and in certain situations may be metastatic lesions with clear documentation why proton beam is being used. The use of proton beam should be heavy on the pediatric patient population. Published literature should be studied very carefully by a task force before adopting every single published paper. We as radiation oncologists have a fiscal responsibility and if we are not careful Proton Beam use is going to be very difficult to sustain at the current levels, then at that point everybody will be hurt. There is no difference in the radiation biology of photons and proton beams. The difference is in the physics; Bragg-Peak and lateral scatter.

Response

We did form a task force perform further work on the document which has resulted in a better document.

11. Comment

GROUP I: is as listed in the proposed policy BUT delete; Extremity Sarcoma.

Response

Extremity sarcoma was removed.

12. Comment

GROUP II Proton Beam Therapy may be used only under the auspices of a clinical trial.

- 1) Malignant lesions of the Paranasal Sinuses, and other accessory sinuses.
- 2) Para- aortic L.Ns in Ca.Cx.
- 3) Pancreatic and adrenal tumors.
- 4) Lung Ca(Small Cell and Non-Small Cell)
- 5) Prostate Ca;

There is yet no good comparative data to determine whether or not Proton Beam Therapy for prostate cancer is superior to IMRT or Brachytherapy. ICD-9 Codes should reflect the above.

Response

This section has been changed.

13. Comment

I would support the use of proton therapy for patients treated in the context of NCI approved cooperative group clinical trials such as those performed by the Radiation Therapy Oncology Group (RTOG). Local clinical studies or registries may usually not qualify as true clinical trials.

Response

We agree that a clinical trial is preferable to a clinical registry but we believe that a registry would have value in reviewing outcomes if set up so that the information could be shared and evaluated. We have decided to include both options

14. Comment

I certainly support the use of proton therapy for pediatric patients requiring craniospinal radiation. This includes mostly children having medulloblastoma, germinoma, or other brain tumors. There are a number of other less common craniospinal indications.

Response

We have added several more types of brain tumors.

15. Comment

Several would support the use of proton therapy for ocular malignancies especially intraocular melanoma.

Response

This is in the policy.

16. Comment

In some of the cases listed, it appears that proton therapy is being indicated as an alternative to radiosurgery technique. I am not aware of any evidence that proton based radiosurgery is superior to LINAC radiosurgery or gamma knife treatment.

Response

This would be considered another treatment option.

17. Comment

I do not support the use of proton therapy for metastatic disease.

Response

This is our policy statement on metastases.

In general, proton beam radiotherapy is not indicated for cancers that are widely disseminated, such as leukemias or malignancies with hematogenous metastases or as a short term palliative procedure. Proton beam therapy is also not indicated in the treatment of very radiosensitive tumors such as lymphomas or germ cell neoplasms. The intent of treatment should be curative. If proton beam radiotherapy is used for a patient with metastatic disease, evidence should be

provided to justify the expectation of a long-term benefit (> 2y), as well as evidence of a dosimetric advantage for proton beam radiotherapy over other forms of radiation therapy.

18. Comment

The types of cancer for which proton therapy will be considered medically reasonable and necessary (Group I) should be further limited. In my opinion group I should include pediatric tumors, chordoma, chondrosarcoma, and intraocular melanoma. All others should be treated as part of a clinical trial and therefore moved to Group II.

Response

We have adjusted the groupings but not as extensively as you suggest.

19. Comment

Group I

I do not support including primary and variant forms of astrocytoma or glioblastoma tumors in the group I list. In some cases pineal gland tumors will require craniospinal radiation for which proton therapy may be superior. Otherwise, there is no evidence that proton therapy is superior for these tumors. In addition the treatment of benign and atypical meningioma with proton therapy should be studied further before inclusion in the group I list. These can be treated with radiosurgical techniques and do not require proton beam. Including rare tumors such as acoustic neuroma, craniopharyngioma, and arteriovenous malformations is not unreasonable. In most cases, these tumors may be adequately treated with current methods including radiosurgery however Pineal tumors are rare and may require craniospinal radiation or radiosurgery.

Response

There are other options as you indicate for treatment of these conditions. We do not want to imply that because a condition is listed in Group I it precludes further trials for these conditions.

20. Comment

Group I

Some pituitary tumors may require craniospinal radiation, most do not. Some pituitary tumors may require radiosurgical technique but not necessarily proton therapy.

Response

True, but if a critical structure is nearby we would not want to preclude its use.

21. Comment

Group I

I would support the use of proton therapy for chordoma and chondrosarcoma based on extensive publications.

Response

Thank you for your comment.

22. Comment

Group I

I do not support including malignant lesions of the head and neck. There is no evidence that proton therapy is better than conventional radiation therapy for this.

Response

This is covered only if there was prior radiotherapy treatment in the same site based on the literature we have received.

23. Comment

Group I

I do not support including lung cancers. There is no evidence that proton therapy is better than conventional radiation therapy for this.

Response

We have placed lung cancer in the Group II section meaning this requires more study.

24. Comment

Group I

I do not support including unresectable retroperitoneal sarcoma and extremity sarcoma. There is no evidence that proton therapy is better than conventional radiation therapy for this.

Response

We have removed extremity sarcoma but will continue to cover retroperitoneal sarcoma.

25. Comment

Group I

There is no evidence that all patients under age 18 would benefit from proton therapy. Since there are relatively few cases, I would support that however.

Response

Thank you for this comment.

26. Comment

Group I

In my opinion the remaining language under group I should be changed. The two statements given leave open the decision for use of proton therapy to clinical opinion as opposed to recognized evidence. Specifically “There is documented clinical rationale that doses thought to be above the level otherwise attainable with other radiation methods might improve control rates”. (Might improve? By how much? With what dose?). These are situations in which actual clinical trials should be done. Similarly “There is documented clinical rationale that higher levels of precision associated with proton beam therapy are clinically necessary”. That would be a clinical trial.

Response

The language in this section has been changed.

27. Comment

Group I

In my opinion, dosimetric criteria alone cannot be used to determine which cases may benefit from proton therapy. One needs to show a clinically relevant endpoint such as increased tumor control or decreased side effects in a randomized controlled trial. Dosimetric criteria are easily manipulated to show slight improvements over 3D conformal radiation or IMRT which are clinically irrelevant. Look for large proton centers to establish automated methods to provide the required documentation. Such constructs as “patient’s record demonstrate why proton beam radiotherapy is considered the treatment of choice” and “dosimetric evidence of reduced normal tissue toxicity” are artificial and cannot be verified.

Response

We have expanded this section to read.

The patient’s record demonstrates why Proton beam radiotherapy is considered the treatment of choice for the individual patient. Specifically, the record must address the lower risk to normal tissue, the lower risk of disease recurrence, and the advantages of the treatment over IMRT or 3-dimensional conformal radiation. Dosimetric evidence of reduced normal tissue toxicity and/or improved tumor control must be maintained

28. Comment

Group II:

These patients would have to be part of a clinical trial in order for treatment to be considered medically reasonable and necessary. I would support any national cooperative group trial of proton therapy. **With respect to prostate cancers, please note there are relatively few stage T3 and T4 cancers treated today. Also there is controversy whether any radiation would benefit patients with node positive prostate cancer.**

Response

Our policy now reads:

The prostate cancer should be locally advanced prostate cancer (T3 or T4) (the tumor has spread through the capsule or has invaded seminal vesicles or other structures) and any N disease (either no spread to lymph nodes or there has been spread to the pelvic lymph nodes Note: Spread beyond pelvic lymph nodes is considered metastatic disease.)

We will be following this closely and will appreciate additional input as the studies come forth.

29. Comment

Finally I did not understand the language: "...factors considered favorable for coverage include enrollment of the patient in an appropriate clinical registry for planned assessment and publication". In my view, a clinical registry is not a clinical trial. A registry is just a list of patient and treatment characteristics and outcomes.

Response

We agree that a clinical trial is preferable to a clinical registry but we believe that a registry would have value in reviewing outcomes if set up so that the information could be shared and evaluated. We have decided to include both options.

30. Comment

The paragraphs under Indications are confusing. The first statement is that proton beam therapy will be considered medically reasonable and necessary for the following conditions. These conditions are listed under Group I. The last paragraph following group I makes a statement "if the above provisions are met and the patient is treated in a protocol, etc."

Does this mean that covered patients must be treated on a protocol, or that if they are treated on a protocol, it must be IRB approved?

Response

Yes, we would expect IRB approval.

31. Comment

From the document, it appears that patients in with conditions listed under Group 2, proton therapy will be considered medically reasonable and necessary if the prior conditions are met and the patients are on a clinical trial.

Response

Yes this is true.

32. Comment

One of the primary tenets of radiation therapy is to increase the therapeutic ratio – that is, to increase the dose to the tumor while limiting the dose to normal tissues. Many of the newer techniques in radiation therapy (intensity-modulated radiation therapy, stereotactic radiation therapy) utilize multiple beams to achieve the dose escalation component, and do this without including large amounts of normal tissues in the high dose area. However, this is accomplished only by spreading the low-to-medium dose region over a larger area, increasing the integral dose. This exposes much more normal tissue to potential toxicity, as well as the risk of second

malignancies. The physical properties of proton therapy allows for dose escalation, without increasing the exposure to normal tissues.

Response

Thank you for this information.

33. Comment

Under Indications and Limitations of Coverage and/or Medical Necessity.

- The third paragraph states "Stereotactic techniques are sometimes used with proton beam therapy especially for skull based, uveal tract tumors and others."

Based on statements in the second paragraph in this section (Proton therapy is of particular value in those tumors located close to serially organized tissues where a small local overdose can cause fatal complications such as most tumors close to the spinal cord), we suggest modifying the sentence above to read "Stereotactic techniques are sometimes used with proton beam therapy especially for skull based, uveal tract tumors, spine tumors and others." This would allow treatment of a primary, recurrent or metastatic spine tumor with stereotactic proton beam therapy in patients with the expectation of long term benefit (> 1 years). Proton beam therapy would be particularly valuable if the patient had been previously treated with x-rays. This rationale seems to be justified as noted under "Indications," "Group 1," #4, "Benign or malignant conditions of the base of skull or axial skeleton [including spine] including but not limited to chordomas and chondrosarcomas."

Response

We have added some of this information.

34. Comment

We would like to request the following changes to the Indications (Group 1):

- #6 "Lung cancers, especially non small cell lung cancer (NSCLC)." We suggest that small cell lung cancer (SCLC) should also be included for the same reasons as NSCLC which include a lower dose to normal lung tissue, heart, esophagus and spinal cord and escalation of dose to the primary tumor and involved lymph nodes (Chang, MD Anderson Cancer Center, 2009).

Response

We have placed all lung cancers in the Group II section and look forward to seeing the results of the clinical trials.

35. Comment

G #8, "Solid tumors in children up to age 18." We propose including lymphomas in order to decrease the risk of radiation-induced malignancies (lung, breast, esophagus, gastric, sarcomas), cardiomyopathy, coronary artery disease, pericarditis with effusion and pulmonary fibrosis as late effects. This would also apply to adults with lymphoma (protons would protect the heart, lung and breast, particularly in young and middle aged adults) (Hoppe, University of Florida, 2010; (Li, MD Anderson Cancer Center, 2010~ Chera, University of Florida, 2009~Schneider, PSI, 2010).

ICD-9 codes that support medical necessity would include 200.00-202.98.

It is our understanding that lymphomas are included in Group 1 in the Highmark Medicare Proton Beam policy L30314 and the Noridian Administrative Services policy for External Beam/Teletherapy L24354.

- The paragraph that reads "If the above provisions are met and the patient is treated in a protocol that is designed for evidence development and for future publication, it is expected that future published data will support an outcome advantage for Medicare patients for continued coverage of the specified diagnosis. The protocol in and by itself does not constitute criteria for coverage.

The presence of an Institutional Review Board (IRB) review when appropriate and patient informed consent are also expected". It is unclear if this paragraph pertains to patients with metastatic lesions or to all patients included in Group 1 conditions. It is our recommendation that this section apply to all indications included in Group 1 and we ask that WPS further clarify this language in the final policy.

Response

36. Comment

With regard to the statement that Proton Beam treatment of the following conditions may be considered medically necessary only if the above criteria are met under the auspices of a clinical trial. (Page 3 of the draft policy). Please comment on specific criteria as this is not clear in the policy.

Response

We would not determine the criteria of a clinical trial. This would be determined by the experts in the area and the information on the topic they determine is essential to pursue to advance the scientific evidence.

37. Comment

We would like to request the following changes to the Indications (Group 2):

- Group 2 provides that proton beam therapy will be considered medically reasonable and necessary for the following conditions.

"Malignant lesions of the paranasal sinus, and other accessory sinuses." We believe these indications should be included with Group 1, category #5 "Malignant lesions of the head and neck" (Chan, Massachusetts General Hospital [MGH], 2010; Fitzek, MGH, 2002; Truong, MGH, 2009; Nishimura, Japan, 2007).

Response

They have been moved to Group I

38. Comment

"Advanced pelvic tumors including malignant lesions of the cervix." We would propose that advanced pelvic tumors include, but not be limited to, endometrial, ovarian, rectal, anal, vulvar, vaginal, and urethral malignancies and sarcomas.

Response

The policy now states:

Advanced stage, unresectable pelvic tumors including those with peri-aortic nodes or malignant lesions of the cervix

39. Comment

"Left breast tumors." We would propose that right breast tumors also be included since these patients have excessive radiation-induced mortality related to contralateral breast cancer, lung cancer, esophageal cancer and sarcomas, especially in younger women (Early Breast Cancer Trialists' Collaborative Group, 2005; Lundkvist, Karolinska Institute, 2005). The three critical structures to be included and spared in the case of right breast tumors include lung, contralateral breast, esophagus and chest wall soft tissues.

Response

We have continued to cover left breast tumors only at this time.

40. Comment

"Skin cancer with perineural/cranial nerve invasion." We would propose that these fall into the category of Group 1, #5. The majority of these cases will be advanced skin cancers arising from the head and neck area and invading the skull base with cranial nerve invasion.

Response

We have decided that we will continue to leave this in Group II.

41. Comment

"Cancers of the lung and upper abdominal/peri-diaphragmatic cancers." We propose that cancers of the lung, including both NSCLC and SCLC, be included in the category of Group 1, #6. We assume that they already are, but would like further confirmation. We would also propose that "g" include, but not be limited to, lymphoma of the mediastinum and/or abdomen, esophageal cancer, and gastric cancer (Li, MD Anderson Cancer Center, 2010; Zhang, MD Anderson Cancer Center, 2008; Isacson, Sweden, 1998; Sugahara, Tsukuba, 2005). In addition, lung cancer is listed in both groups 1 & 2 but we believe lung cancer should be in group 1 as protons have a major influence on lessening severe toxicity and improving tumor control and survival (Chang, MD Anderson Cancer Center, 2009).

Response

We have placed all lung cancers in Group II.

42. Comment

We propose that the following ICD-9 codes be included in Group 1, #5, Malignant lesions of the head and neck:

140.0-140.9 (lip),
141.0-141.9 (base of tongue/tongue),
142.0-142.9 (parotid gland/salivary gland),
143.0-143.9 (gum),
144.0-144.9 (floor of mouth),
145.0-145.9 (cheek/mouth),
146.0-146.9 (tonsil/oropharynx),
147.0-147.9 (nasopharynx),
148.0-148.9 (posterioricoid/hypopharynx),
149.0-149.9 (pharynx/lip/oral cavity),
160.0-169.0 (nasal cavity/accessory sinus),
161.0-161.9 (glottis/larynx),
165.0-165.9 (upper respiratory tract),
173.0-173.9 (skin of lip), and
193 (thyroid gland).

See Liebsch, MGH, 2004; Slater, LLUMC, 2005.

We propose the following ICD-9 codes also be included in Group 1:

200.00-202.98 (reticulosarcoma, lymphoid and histiocytic tissue) for the reasons stated previously.

We propose the following ICD-9 codes also be included in Group 1, #6, Lung cancers:

162.0-162.9 (trachea/bronchus),
163.0-163.9 (parietal pleura), and
164.0-164.9 (thymus/mediastinum).

Heart, lung, esophagus and spinal cord will all be exposed to a lower dose when treated with protons.

Response

We have reviewed this code request. Some of these codes will be included in the document.

43. Comment

We propose the following ICD-9 codes also be included in Group 1:

200.00-202.98 (reticulosarcoma, lymphoid and histiocytic tissue) for the reasons stated previously.

Response

We received information not to include 200.00-202.98 at this time.

44. Comment

We propose the following ICD-9 codes also be included in Group 1, #6, Lung cancers:

162.0-162.9 (trachea/bronchus),

163.0-163.9 (parietal pleura), and

164.0-164.9 (thymus/mediastinum).

Heart, lung, esophagus and spinal cord will all be exposed to a lower dose when treated with protons.

Response

We have included codes 162.2 – 162.8 (malignancy of lung and bronchus) in Group II.

45. Comment

We did not see ICD-9 codes for Group 1, #2, intraocular melanomas or Group 1, #8, solid tumors in children up to age 18, retinoblastoma and these should be included as well (Char, University of California, San Francisco and Berkeley, 1993; Damato, United Kingdom, 2005; Gragoudas, MGH, 2006; Dendale, France, 2006; Muzemider, MGH, 2001; Lee, MD Anderson Cancer Center, 2005; Krengli, MGH and MD Anderson Cancer Center, 2005).

Response

These codes are in the policy as Group I codes. 190.0 - 190.9

46. Comment

In conclusion, we appreciate WPS analyzing the above information and modifying the draft LCD so that beneficiaries afflicted with cancer, regardless of tumor site are afforded the same treatment options and that there is reasonable coverage for these services. We have included numerous evidence based articles supporting this request for the expansion of coverage. We believe this draft policy to be very similar to the First Coast Service Options (FCSO) policy except that FCSO provides for the use of proton beam therapy for prostate cancer. We believe the proposed changes will make the WPS draft policy consistent with other Medicare contractor policies. We would like to see consistency between the Nordinian policy and the WPS policy as it allows patients consistent coverage between hospital and physician services.

Response

Thank you for your comments. We cannot find a Nordinian policy on this topic.

47. Comment

Group 1

1. Benign or malignant central nervous system tumors to include but not limited to primary and variant forms of astrocytoma, glioblastoma, medulloblastoma, acoustic neuroma, craniopharyngioma, benign and atypical meningiomas, pineal gland tumors, and **arteriovenous** malformations

2. Intraocular melanomas

3. Pituitary neoplasms

4. Benign or malignant conditions of the base of the skull or axial skeleton including but not limited to chordomas and chondrosarcomas

5. Malignant lesions of the head and neck

6. Lung cancers, especially NSCLC.

7. Unresectable retroperitoneal sarcoma and extremity sarcoma

8. Solid tumors in children up to age 18

In addition, Proton Beam Therapy is indicated when:

- The Dose Volume Histogram (DVH) illustrates at least three (3) critical structures or organs protected by the use of Proton Beam Therapy;

Comment: Does this mean that for Group 1 diagnoses, a comparison of proton versus x-ray plans are needed to verify sparing of critical structures?

What if there is sparing of one major critical structure, such as the eye or brainstem? This should be enough to justify protons.

- The dose to control or treat the tumor cannot be delivered without exceeding the tolerance of the normal tissue;

- There is documented clinical rationale that doses generally thought to be above the level otherwise attainable with other radiation methods might improve control rates; or

- There is documented clinical rationale that higher levels of precision associated with Proton Beam Therapy compared to other radiation treatments are clinically necessary.

- For the treatment of primary lesions, the intent of treatment must be curative - For the treatment of metastatic lesions, there must be the expectation of a long-term benefit (> 2y) that could not have been attained with conventional therapy

Please clarify whether just one or all of above criteria must be satisfied

Response

This has been changed to read:

The Dose Volume Histogram (DVH) one or more critical structures or organs protected by the use of Proton Beam Therapy;

- The dose to control or treat the tumor cannot be delivered without exceeding the tolerance of the normal tissue;

- There is documented clinical rationale that doses generally thought to be above the level otherwise attainable with other radiation methods might improve control rates; or

- There is documented clinical rationale that higher levels of precision associated with Proton Beam Therapy compared to other radiation treatments are clinically necessary.

48. Comment:

b. the expectation of a complete eradication of the metastatic lesion that could not have been safely accomplished with conventional therapy, as evidenced by a dosimetric advantage for proton beam radiotherapy over other forms of radiation therapy

- The patient's record demonstrates why Proton beam radiotherapy is considered the treatment of choice for the individual patient. Specifically, the record must address the lower risk to normal tissue, the lower risk of disease recurrence, and the advantages of the treatment over IMRT or 3-dimensional conformal radiation. Dosimetric evidence of reduced normal tissue toxicity and/or improved tumor control must be maintained.

Please clarify whether just one or all of the DVH and following criteria must be satisfied.

If the above provisions are met and the patient is treated in a protocol that is designed for evidence development and for future publication, it is expected that future published data will support an outcome advantage for Medicare patients for continued coverage of the specific diagnosis. The protocol in and by itself does not constitute criteria for coverage. The presence of

an Institutional review Board (IRB) review when appropriate and patient informed consent is also expected.

Response

The section now reads:

The expectation of a complete eradication or improved duration of control of the metastatic lesion that could not have been safely accomplished with conventional therapy, as evidenced by a dosimetric advantage for proton beam radiotherapy over other forms of radiation therapy.

- The patient's record demonstrates why Proton beam radiotherapy is considered the treatment of choice for the individual patient. Specifically, the record must address the lower risk to normal tissue, the lower risk of disease recurrence, and the advantages of the treatment over IMRT or 3- dimensional conformal radiation. Dosimetric evidence of reduced normal tissue toxicity and/or improved tumor control must be maintained.

If the above provisions are met and the patient is treated in a protocol that is designed for evidence development and for future publication, it is expected that future published data will support an outcome advantage for Medicare patients for continued coverage of the specific diagnosis. The protocol in and by itself does not constitute criteria for coverage. The presence of an Institutional Review Board (IRB) review when appropriate and patient informed consent are also expected.

49. Comment: The support for patients on clinical trials, including registries directed towards publication, is to be commended. This is the best only mechanism by which the benefit protons can be validated. We expect that most or almost all of our patients will be treated on a protocol, intended to analyze toxicity *and/or* compare tumor control rates.

However, what information from protocols are you requesting? Whether or not a patient is on protocol? That we forward abstract or manuscript results as they become available? It is unclear how this paragraph impacts the coverage decision.

Proton beam treatment of the following conditions may be considered medically reasonable and necessary only if the above criteria are met under the auspices of a clinical trial.

Response

We will not be requesting information from the protocols. We would expect that this information be compiled and kept in a database maybe managed by your institution and or society and made available through means available to you. You need only to tell us through the use of modifiers whether the service is being performed under the auspices of a clinical trial.

50. Comment:

Health care costs have been rising and are expected to continue to rise well above the annual inflation rate. In this current time of austerity it is clear that health care dollars should be spent with careful analysis of cost & benefit. Failure of health care providers to do so voluntarily will force the government, without any doubt, to apply across the board reductions that might be financially devastating to many providers. It is very important that we "police ourselves".

Proton therapy is several times more expensive than conventional linear accelerator based radiation therapy and therefore before we commit our scarce financial resources to this new technology it is critical to demonstrate clear clinical benefits that justify the additional expense. I have reviewed the provided list of possible applications of proton therapy and I estimate that this list would encompass about 1/2 to 2/3 of all cases seen in an average radiation oncology department. This is simply unaffordable and unreasonable.

A more logical approach is to classify potential treatment sites into 2 categories.

Category A: Which represents diseases with common incidence and therefore national randomized clinical trials can be conducted to measure clinically meaningful, and not dosimetric subtle benefit, end points. Examples of this class would be prostate cancer, non-small cell lung cancer, head and neck cancer and glioblastoma multiformae.

Category B: Would represent diseases of uncommon occurrence for which it is not possible to measure improved outcome by conducting randomized clinical trials. The value of proton therapy in treating these diseases can be studied by rigorous phase II studies.

In either case we strongly suggest that CMS would pay only for patients treated by proton therapy in the context of NCI approved trials.

Response

We support your view that clinical trials are needed for many of the indications listed.

51. Comment

In Indications, Group 1, #5 lists “malignant lesions of the head and neck”, but in the ICD-9 Codes that support medical necessity section under Group 1, the only head and neck cancer diagnosis group listed is 171.0-171.9: malignant neoplasm of connective and other soft tissue of head, face and neck.

Response

We have added additional codes for head and neck cancers.

52. Comment

In the narrative section of Indications, Group 1 it states, “Proton beam treatment of the following conditions may be considered medically reasonable and necessary only if the above criteria are met under the auspices of a clinical trial.” If you refer to the Highmark Medicare Services LCD L30314-Proton Beam Therapy for the following jurisdictions: Pennsylvania, Maryland, District of Columbia, New Jersey and Delaware, there is no such separation of diagnoses. This non-separation is what I am requesting for the WPS Proton policy.

Response

We have given Highmark’s policy consideration in developing our local policy.

53. Comment

I request that the WPS proposed DRAFT LCD for Proton Beam Therapy resemble LCD L30314 mentioned above. Include the following diagnoses in the codes that support medical necessity and remove from the Group 2 section in the WPS Draft Proton Policy:

- 140.0-140.9: malignant neoplasm of upper lip, vermilion border
- 141.0-141.9: malignant neoplasm of base of tongue
- 142.0-142.9: malignant neoplasm of parotid gland
- 143.0-143.9: malignant neoplasm of upper gum
- 144.0-144.9: malignant neoplasm of anterior portion of floor of mouth
- 145.0-145.9: malignant neoplasm of cheek mucosa
- 146.0-146.9: malignant neoplasm of tonsil
- 147.0-147.9: malignant neoplasm of superior wall of nasopharynx
- 148.0-148.9: malignant neoplasm of postericoid region of hypopharynx

- 149.0-149.9: malignant neoplasm of pharynx
- 150.0-150.9: malignant neoplasm of cervical esophagus

151.0-151.9: malignant neoplasm of cardia
152.0-152.9: malignant neoplasm of jejunum
153.0-153.9: malignant neoplasm of hepatic flexure
154.0-154.8: malignant neoplasm of rectosigmoid junction
155.0-155.2: malignant neoplasm of liver primary
156.0-156.9: malignant neoplasm of gallbladder
157.0-157.9: malignant neoplasm of head of pancreas
159.0-159.9: malignant neoplasm of intestinal tract
160.0-160.9: malignant neoplasm of nasal cavities
161.0-161.9: malignant neoplasm of glottis
162.0-162.9: malignant neoplasm of trachea
163.0-163.9: malignant neoplasm of parietal pleura
164.0-164.9: malignant neoplasm of thymus
173.0-173.9: other malignant neoplasm of skin of lip
174.0-174.9: malignant neoplasm of nipple and areola of female breast
175.0-175.9: malignant neoplasm of nipple and areola of male breast
179.-184.9: malignant neoplasm of uterus
185: malignant neoplasm of prostate
186.0-186.9: malignant neoplasm of undescended testis
187.1-187.9: malignant neoplasm of prepuce
188.0-188.9: malignant neoplasm of trigone of urinary bladder
189.1.-189.9: malignant neoplasm of renal pelvis
193: malignant neoplasm of thyroid
197.7: malignant neoplasm of liver-secondary

Response

We have included many of the coding suggestions above in the policy. We will continue to have Group I and Group II categories listed on the policy until the literature supports general coverage.

61. Comment

Indications, Group 1, #5 lists “malignant lesions of the head and neck”, but the ICD-9 Codes that support medical necessity section under Group 1 is incomplete. The only head and neck cancer diagnosis group listed is 171.0-171.9: malignant neoplasm of connective and other soft tissue of head, face and neck. I request the diagnoses of 140.0-149.9 and 160.0-173.9 to be included.

Response

We do include more options for head and neck malignancies but will not include 140.0-149.9 and 160.0-173.9 at this time.

62. Comment

Indications, Group 1, #6 lists “lung cancers, especially NSCLC”, but in the ICD-9 Codes that support medical necessity section under Group 1, lung cancer 162.0-162.9 are not listed as covered diagnoses.

Response

Lung cancer has been moved to Group II and these diagnosis codes are included there.

63. Comment

Adoption of a policy similar to LCD L30314 would include the ICD-9 codes mentioned above as well as the following:

150.0-150.9: malignant neoplasm of cervical esophagus
151.0-151.9: malignant neoplasm of cardia
152.0-152.9: malignant neoplasm of jejunum

153.0-153.9: malignant neoplasm of hepatic flexure
154.0-154.8: malignant neoplasm of rectosigmoid junction
155.0-155.2: malignant neoplasm of liver primary
156.0-156.9: malignant neoplasm of gallbladder
157.0-157.9: malignant neoplasm of head of pancreas
159.0-159.9: malignant neoplasm of intestinal tract
174.0-174.9: malignant neoplasm of nipple and areola of female breast
175.0-175.9: malignant neoplasm of nipple and areola of male breast
179.-184.9: malignant neoplasm of uterus
185 malignant neoplasm of prostate
186.0-186.9: malignant neoplasm of undescended testis
187.1-187.9: malignant neoplasm of prepuce
188.0-188.9: malignant neoplasm of trigone of urinary bladder
189.1.-189.9: malignant neoplasm of renal pelvis
193: malignant neoplasm of thyroid
197.7: malignant neoplasm of liver-secondary

A policy consistent with the Highmark would include these diagnoses without the qualifier of a clinical trial.

Response

We have included many of these conditions in the policy. We believe the qualifier of a clinical trial is appropriate.

64. Comment

The Consortium is concerned with some critical language in the draft LCD: *"Proton beam treatment of the following conditions may be considered medically reasonable and necessary only if the above criteria are met under the allspices of a clinical trial."* We would like to see a clear definition of what is meant by "clinical trial." In our opinion, a clinical trial, in this context, should include all types of clinical trials, studies, and registries. We agree that it would be appropriate to collect further information on patients who fall into Group 2 of the draft LCD and support the idea that it would be in the interest of all patients to be enrolled in a registry. To that end, ProCure has established the Proton Collaborative Group (PCG). The intention of the PCG is to build the infrastructure necessary to facilitate training, creating and maintaining treatment protocols and enrolling all patients in a registry to conduct protocol and disease specific prospective observational studies of patients treated with proton therapy, in order to track outcomes. All ProCure administered sites and the University of Pennsylvania's Roberts Proton Therapy Center participate in this linked collaborative that will also allow for access to UPENN's research protocols.

Response

While we will allow registries we also would expect clinical trials be pursued to advance the knowledge base on this type of cancer treatment. Group II cancers treatment cannot move to Group I status without clinical trials which are reported in peer-reviewed literature. Registries will not provide the science necessary to match a clinical trial.

PROSTATE CANCER

1. Comment

The draft of policy for coverage of proton beam therapy: is acceptable with the caveat that prostate cancer should definitely remain in Group I. There are more and more data to support the equivalence of outcomes (biochemical disease free survival) with proton therapy for prostate cancer. The major difference now is the decrease in the toxicity profile of proton therapy over conventional radiation modalities such as even IMRT. The data recently published (from the

PROG 95-09 study in the Journal of Clinical Oncology 2010) reveals a 1-2% rectal toxicity rate as opposed to 10-30% rectal injury rate with IMRT and Conformal radiation therapy's historical data. There are also data from Mass General (Harvard Cyclotron) that reveals an increased rate of second cancers of 11-15% versus 6% for proton treated patients (with background cancer rates of 4%). For all those reasons (and even more if you care for me to elaborate), I feel strongly that protons remain a primary option for treatment of early stage/low risk to high risk non-metastatic prostate cancer.

Response

We are pleased to see literature arising on proton beam therapy for prostate cancer.

2. Comment

By all accounts, proton therapy fits this definition of 'better therapy'. In virtually every clinical scenario, proton therapy delivers 60%-80% less dose to the healthy surrounding tissues when compared to photons. Prostate treatments with protons are no exception. The amount of radiation delivered to the healthy rectum and bladder are significantly lower with proton. The phase 3 dose escalation trial by Zietman et al demonstrated the highest PSA free survival (98% in 5 years) reported in any randomized trial. They also demonstrated no differences in rectal and bladder side effects when the radiation dose was increased from 70 CGE to 78 CGE. Recently, University of Florida (Mendenhall et al) reported their proton experience with low risk prostate cancers. They reported 100% PSA free survival at 2 years. In addition, men < 55 years old noted no increased risk for impotence. Unlike protons, photon dose escalation studies have shown higher complications rates, reflecting the higher collateral damage from the higher radiation dose (pollack et al). With higher radiation exposure with photons, risks for radiation induced malignancy are also increased. Chung et al. performed a retrospective cohort study of 503 patients treated at Harvard for protons against a matched SEER cohort. Those treated with X-rays experienced double the rate of secondary malignancies than those treated with protons (12.8% versus 6.4%).

In summary, proton therapy is by definition 'better therapy'. I hope that WPS Local Coverage Determination (LCD) on Proton Beam Therapy would reconsider its stance on prostate cancer and its description of data requirements for coverage of Group II sites.

Response

As with all cancers listed in Group II, as soon as sufficient literature is presented we can reconsider prostate cancer's placement in this policy.

3. Comment

With prostate cancer, developing some form of registry would be considerably helpful in the long run. Certainly it will take some time but will be well worth the effort (if at all possible). I am not certain how a particular prostate cancer case can be selected for proton therapy. It is a big effort challenge discussing all the options and associated details now. For the more aggressive and/or locally advanced presentation proton therapy may be most beneficial. But this division of which case is appropriate will lead to confusion and frustration. The 'registry' format may help if developed and lead to some conclusion to the appropriate use of proton therapy. As to guidelines for prostate cancer (stage, grade, PSA, etc.), the NCCN guidelines may serve as a good baseline. Documentation based on such criteria may provide a nice mechanism for a 'registry' format.

Response

We agree that the NCCN guidelines serve as a good baseline.

4. Comment

I find this draft policy quite appropriate and evidence-based, with the exception of excluding early stage prostate cancer (stages T1c-T2c) from group I coverage. As you are well aware, with

the long term publication of the PROG 9509 phase III randomized study (Zietman et al, Journal of Clinical Oncology 2010, Talcott et al, JAMA 2010), high-dose proton beam therapy has become an accepted and often preferred standard of care for early stage prostate cancer. While several other randomized trials have also shown increased cure rates with high dose *photon (x-ray)* therapy, these improvements have uniformly been offset by increased permanent morbidity. As demonstrated by the above PROG study however, proton beam therapy is the only external beam modality to have demonstrated (by level I evidence) increased cure rates for early stage prostate cancer without added toxicity. It would thus be appropriate that early stage prostate cancer be included under group I coverage for proton beam therapy.

Response

We have received expert advice on the stages of prostate cancer that should be treated with proton beam therapy and they have extended from early to late cancers. For now we intend to cover it for:

“The prostate cancer should be locally advanced prostate cancer (T3 or T4) (the tumor has spread through the capsule or has invaded seminal vesicles or other structures) and any N disease (either no spread to lymph nodes or there has been spread to the pelvic lymph nodes Note: Spread beyond pelvic lymph nodes is considered metastatic disease.)”

5. Comment

I would like you to reconsider coverage of low and intermediate risk prostate cancer patients for proton coverage in the upcoming policy. There has been published data supporting its use for all risk groups showing improved quality of life and excellent control rates. Please don't deny those men diagnosed with lower risk disease the opportunity of the best radiation option available to patients right here in their own backyard.

Response

See number 4 above.

6. Comment

I have an opportunity to review the draft WPS Local Coverage Determination policy on Proton Therapy. I feel that it for the most part it adequately outlines most medical situations in which proton beam therapy is medically reasonable which exception to reference of prostate cancer treatment.

I feel that there is data to reasonably contradict the statement below from the draft policy:

"There is as yet no good comparative data to determine whether or not Proton Beam Therapy for prostate cancer is superior, inferior, or equivalent to external beam radiation, IMRT, or brachytherapy in terms of safety or efficacy."

There are clinical randomized trials that have shown the benefit of dose escalation in prostate cancer in terms of improved cure rates. These trials have shown increased complication rates with dose escalation with exception of the PROG 95-09 (which is a Phase III dose escalation trial)

I feel that the data of supporting increased cure rates and increased complications in patient treated with dose escalation for prostate cancer with the use of photon beam radiation treatment further supports the data showing no increased complications in patients treated with proton beam therapy for early stage prostate cancer.

Please consider these comments and the data when finalizing the draft WPS Local Coverage Determination policy on Proton Therapy document as I feel (and data supports) that early stage

prostate cancer patient will benefit from this treatment modality and should be included under group 1.

Response

We will accept any new clinical trials published in peer-reviewed journals that support the stage, type, effectiveness, and other factors related to treatment of prostate cancer. The literature is starting to come forth but is not complete as yet.

7. Comment

We take exception to the statement that "There is as yet no good comparative data to determine whether or **not Proton Beam Therapy for prostate cancer** is superior, inferior, or equivalent to external beam radiation, IMRT, or brachytherapy in terms of safety or efficacy. We have included evidence based documents supporting the statement that proton beam therapy for prostate cancer is at least equivalent to, if not superior to, external beam and IMRT (Zietman, MGR and Lorna Linda University Medical Center [LLUMC], 2010; Slater, LLUMC, 2004).

Furthermore, there are opportunities to hypofractionate the proton beam therapy which could result in a treatment course with significantly fewer treatments and therefore lower costs similar to or less than IMRT. Patients with T3 or T4 disease with nodal metastases are not ideal candidates for hypo fractionated treatment with proton beam therapy.

Patients with T1 and T2 tumors at intermediate or high risk for recurrence and a prostate cancer related death (young men, high PSA, high Gleason score) are more optimal candidates for proton beam clinical trials. We would propose the inclusion of T1 and T2 primary tumors with intermediate to high risk features.

Although the draft LCD for Proton Beam Therapy does include indications for the use of proton beam therapy in patients with prostate cancer, the rationale for its inclusion in Group 2 is not expressed in the document. The information presented is at odds with fundamental concepts that provide the foundation for high-dose conformal radiotherapy.

It also does not account for the trajectory of research founded on the concept of hypo fractionation (that is, higher dose per fraction with a lesser number of treatment fractions) and the lowest possible dose (to non-target tissues) that forms the cornerstone of radiation protection.

We propose the final policy include the following language for Prostate Cancer coverage.

Multiple lines of medical research demonstrate that higher radiation doses directed to the prostate improves cancer control (Zietman, MGH and LLUMC, 2010; Peeters, Dutch Trial, 2006). However, surrounding organs are also exposed to higher radiation doses, and this increases the rate of complications/adverse effects. Complications limit increasing radiation doses to provide optimal cancer control rates. Incidental radiation exposure of organs surrounding the prostate is associated with increased rates of bladder, colorectal and sarcomatous malignancies.

The volume of irradiated tissue is reduced with proton beam therapy (and brachytherapy) as compared to external beam radiation or IMRT (i.e., teletherapy).

Medical research is evolving toward hypofractionation (administration of higher radiation doses per treatment fraction with a lesser number of treatment fractions) and/or stereotactics with external beam radiation or IMRT. This mimics the process associated with brachytherapy, which cannot be used in all patients with prostate cancer (e.g., unsuitable for anesthesia, urinary obstruction, etc.).

We suggest that the coverage and payments of Proton Beam Therapy for prostate cancer require all of the following:

- a. Physician documentation of prostate biopsy diagnosis and stage;
- b. Documentation and verification that the patient was informed of the range of therapy choices, including risks and benefits; and

c. Documentation of the specific reasons why Proton Beam Therapy was the treatment of choice for the specific patient with regard to at least one of the following:

- Personal risk factors (e.g., smoking history, bladder in situ urothelial malignancy) for or a family history of bladder cancer and a life expectancy of at least ten (10) years.
- Personal risk factors (e.g., adenomatous polyps) for or a family history of colorectal cancer and a life expectancy of at least ten (10) years.
- Planned administration of teletherapy radiation doses greater than standard guidelines (e.g. greater than 75 Gy) when delivered in once daily dose fractions of 2.1 Gy or less and that incorporate image-guidance (e.g., markers, transponders).
- Planned administration of teletherapy radiation doses that use hypofractionation (e.g., fractionated dose of 2.5 Gy or greater) as all or part (i.e., boost) of the treatment regimen and that incorporate image-guidance (e.g., markers, transponders).

Other factors considered favorable for coverage include enrollment of the patient in an appropriate clinical registry for planned assessment and publication.

If the patient cannot clearly meet the criteria for coverage but desires proton beam radiotherapy based on a marketed theoretical advantage, the claim should be billed with the appropriate modifier appended to the treatment delivery code.

Response

We have included many of your suggestions in the policy and are pleased to receive the other information.

8. Comment

i. Prostate Cancer

There is, as yet, no good comparative data to determine whether or not Proton Beam Therapy for prostate cancer is superior, inferior, or equivalent to external beam radiation, IMRT, or brachytherapy in terms of safety or efficacy.

The prostate cancer should be locally advanced prostate cancer (i.e., Stages C or D1 [without distant metastases], also classified as T3 or T4) (the tumor has spread through the capsule on one or both sides but has not invaded seminal vesicles or other structures) and any N disease (either no spread to lymph nodes or there has been spread to the regional lymph nodes Note: Spread beyond local lymph nodes is considered metastatic disease.

Comment: The publications for prostate cancer have been for patients with T1 and T2 NO disease, not patients with T3, T4, or node positive disease. Please clarify whether T1 or T2 patients, both on or off clinical trials, are excluded.

Coverage and payments of Proton Beam Therapy for prostate cancer will require:

- a. Physician documentation of patient selection criteria (stage and other factors);
- b. Documentation and verification that the patient was informed of the range of therapy choices, including risks and benefits; and
- c. Documentation of the specific reasons why Proton Beam was the treatment of choice for the specific patient.

Other factors considered favorable for coverage include enrollment of the patient in an appropriate clinical registry for planned assessment and publication. If the patient cannot clearly meet the criteria for coverage but desires Proton beam radiotherapy based on a marketed theoretical advantage, the claim should be billed with the appropriate modifier appended to the treatment delivery code.

Response

Please clarify whether T1 or T2 patients, both on or off clinical trials, are excluded.

T1 or T2 patients could be part of clinical trials however there are more pressing questions related to early stage prostate cancer. Because these stages are not listed in our policy does not preclude investigation into the best treatments for prostate cancer.

9. Comment

I do feel strongly that proton treatment needs to be limited to T3 and T4 prostate cancer.

There are several reasons for limiting Proton therapy for prostate cancer to T3 and T4 tumors:

a. There is no consensus in the medical literature whether we even need to treat certain patients with prostate cancer. As the policy as written, has no age or performance status limits, would subject persons with questionable benefit to a (most likely non-randomized) clinical trial.

b. As discussed, we have always subjected new technology to more rigorous criteria, mostly to treat harder to cure tumors. For example, IMRT was used to treat head and neck cancer initially, only later did we allow IMRT to be used for prostate and breast, and now we still do not use IMRT for lung cancers for the most part because it is technically difficult to do. T3 and T4 prostate cancers are harder to control locally than T1 and T2. Therefore a trial will give us an idea of proton's efficacy.

c. As noted, the long-term side effects of proton therapy are not known. Loma Linda has treated at least 2000 patients with proton beam since the mid 1990s with good results. Mass. General has also used protons as a boost since the 1980s. However, the numbers are still too small to realize what long-term effects of proton therapy has on patients.

Response

We agree with your assessment.

10. Comment

“Furthermore, the draft LCD appears to rely on an impermissible standard of comparative effectiveness. Specifically, the draft states that “[t]here is as yet no good comparative data to determine whether or not Proton Beam Therapy for prostate cancer is superior, inferior, or equivalent to external beam radiation, IMRT, or brachytherapy in terms of safety or efficacy.” This implies that WPS has inappropriately created and applied a requirement that a service or product have comparative data vis-à-vis some or all other possibly alternative treatments. Medicare procedures for promulgating LCDs do not include any requirements for comparative effectiveness reviews. In fact, a recent meeting of the MEDCAC on treatments for early stage prostate cancer concluded that there was little good evidence comparing any of the major treatment modalities.³

Further reinforcing a belief that WPS employed this impermissible standard is that there is no content within the draft LCD that shows that its determinations are based on evidence or permissible factors for limiting coverage to a treatment that has substantial evidence of its safety and effectiveness. In fact, there is a significant literature that shows that, indeed, proton therapy is a highly effective treatment for prostate cancer in terms of safety and efficacy. That literature shows outcomes that are certainly equivalent to other modalities and, arguably superior. For prostate cancer, for example, 2008 corrected data from the Zietman et al. Phase III prospective dose escalation trial using protons to dose escalate⁴ shows 98 percent freedom from biochemical failure (“FFBF”) at 5 years for low-risk prostate patients. That is a 59 percent reduction in FFBF from those treated with the conventional dose of photon therapy. Toxicity outcomes show a 90 percent reduction in those with \geq Grade 3 GI toxicities compared to similar

Phase III dose escalation trial by Pollack et al. using 3D conformal photons to dose escalate.^{5 – 3}

Most recently, Talcott and other reported that long term results from those receiving high dose proton therapy showed no increase in patient reported outcomes compared to lower doses.⁶ This result further reinforces the benefits of proton therapy for localized prostate cancer in its ability to deliver clinically effective doses without increased toxicity. Also, Nihei and others published findings that confirm that proton therapy for localized prostate cancer can achieve a low incidence of late Grade 2 or greater rectal toxicities.⁷ This was done in a multi-institutional prospective study.

Third, the draft does not contain anything but the most cursory discussion of proton therapy and its application to the disease conditions affected by the draft LCD. For example, the draft LCD proposes to cover proton therapy for localized prostate cancer only as part of a clinical trial. There is no discussion of why such a conclusion was reached. “

Fourth, the draft LCD should be withdrawn because it fails to clearly define the conditions under which it will cover proton therapy for prostate cancer. The draft LCD provides that proton beam treatment of prostate cancer “may be considered medically reasonable and necessary only if the above criteria are met under the auspices of a clinical trial.” The draft LCD does not contain a definition of what is meant by “clinical trial.” The Consortium believes that prostate cancer should be covered outside of a clinical trial, as there is sufficient evidence for proton therapy as reasonable and necessary. According to four dose escalation trials, proton delivers a higher dose to the tumor safely and results in superior control rates.⁸ Proton therapy significantly reduces the dose to the pelvis and rectum, lowering such side effects as – 4 –

The Consortium believes that prostate cancer should be covered outside of a clinical trial, as there is sufficient evidence for proton therapy as reasonable and necessary. According to four dose escalation trials, proton delivers a higher dose to the tumor safely and results in superior control rates. Proton therapy significantly reduces the dose to the pelvis and rectum, lowering such side effects as nausea, vomiting, bowel holes, rectal bleeding and rectum tumors.² Only covering patients in clinical trials would essentially equate to coverage with evidence development for patients with prostate cancer - a disease site with adequate supporting evidence. Requiring additional evidence would be unfair to patients who should be eligible for proton treatment and it would place an undue burden on the medical centers that treat with protons. In summary, the Proton Therapy Consortium agrees with WPS's decision to cover proton therapy for Groups 1 and 2 as outlined in the draft LCD with the exception of prostate. We request that you add clarifying language to what is meant by a clinical trial and move prostate to coverage **Group!**.

Response

The NCCN guidelines indicate that proton therapy is not indicated for routine use at this time. Many of the literature articles presented indicate further studies are needed. It is unfortunate that there was little good evidence comparing any of the major treatment modalities for prostate cancer. The fact that we are promoting (albeit in a small way) more research should be considered a positive step

OTHER

1. Comment

The Consortium views the rationale for issuing this draft LCD as confusing and potentially legally compromising in a number of ways. As further described below, these flaws are so significant that it is impossible for interested parties to provide meaningful substantive comments. Some of these issues deserve clarification while others require substantial correction. For these reasons as described in detail below, we respectfully urge WPS to withdraw the draft and we offer to work with WPS should it decide to reissue a draft LCD.

First, the draft does not provide any explanation for the revision of this policy. It may be, as hinted at in the revision history and explanations provided in corresponding draft LCDs for WPS's MAC Part A and Part B States and WPS's legacy states, that the intent of this draft is to consolidate policies in conformance with the CMS Medicare Administrative Contractor Workload Implementation Handbook ("Workload Handbook"). That is, WPS is removing the states of Delaware, District of Columbia, Maryland, New Jersey and Pennsylvania because these states are transitioning to the MAC Part A contractor Highmark.

Response

This is a new policy. This policy will have no impact on the above mentioned states. Those states are subject to the policies issued by contractors in those states. Our current jurisdictions are:

Primary Geographic Jurisdiction

Carrier B: Wisconsin, Illinois, Michigan, Minnesota

Fiscal Intermediary A:

Fiscal Intermediary A: Alaska, Alabama, Arizona, Arkansas, Connecticut, Florida, Georgia, Iowa, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Massachusetts, Maine, Michigan, Minnesota, Missouri, Mississippi, Montana, North Carolina, North Dakota, Nebraska, New Hampshire, Ohio, Oregon, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Virginia, Vermont, Washington, Wisconsin, West Virginia, Wyoming, U.S. Virgin Islands

MAC A/B: Iowa, Missouri, Nebraska, Kansas

2. Comment

Importantly, however, according to the CMS Handbook, the contractor "must select the least restrictive or most clinically appropriate LCD from the existing LCDs on a single topic."¹

Response

The above relates to transitioning to a new contractor. This policy is new for jurisdictions J5, Legacy B and Legacy A. It is not a transitioning document.

Many of the Proton Beam facilities are free standing (not considered part of a hospital) so Part a payment mechanisms would not necessarily be in place for those facilities.

3. Comment

Beyond this, the draft fails to make clear what, if any, criteria were used in making its determination to promulgate this draft LCD. The draft makes no reference to criteria and, significantly, makes no reference to the criteria for when to develop an LCD as contained in section 13.4 of Chapter 13 of the Medicare Program Integrity Manual. Without such an explanation, it appears that it promulgating a draft LCD on this topic is inappropriate. At a

minimum, without such an explanation, it is not possible to provide comments on whether the creation of the draft is necessary. 1 Workload Handbook (Legacy-to MAC). Updated September 10, 2010. p 4-7. – 2 – “

Response

We are meeting all criteria required to create a new draft policy. Proton Beam therapy is considered new technology and even though it has been around for years in some areas it will be new to our jurisdictions. New technology is one of the reasons listed in Chapter 13 of the Medicare Program Integrity Manual. We quote:

13.4 - When To Develop New/Revised LCDs

(Rev. 71, 04-09-04)

The use of a LCD helps avoid situations in which claims are paid or denied without a provider having a full understanding of the basis for payment and denial.

A. Contractors Shall Develop New/Revised LCDs

Contractors shall develop LCDs when they have identified a service that is never covered under certain circumstances and wish to establish automated review in the absence of an NCD or coverage provision in an interpretive manual that supports automated review.

B. Contractors May Develop New/Revised LCD

Contractors have the option to develop LCDs when any of the following occur:

A validated widespread problem demonstrates a significant risk to the Medicare trust funds (identified or potentially high dollar and/or high volume services); See Chapter 3, § 3.2A, Error Validation Review, for an explanation of the problem validation process. Multi-state contractors may develop uniform LCDs across all its jurisdictions even if data analysis indicates that the problem exists only in one state.

A LCD is needed to assure beneficiary access to care.

A contractor has assumed the LCD development workload of another contractor and is undertaking an initiative to create uniform LCDs across its multiple jurisdictions; or is a multi-state contractor undertaking an initiative to create uniform LCDs across its jurisdiction; or

Frequent denials are issued (following routine or complex review) or frequent denials are anticipated.

“13.5.1 - Reasonable and Necessary Provisions in LCDs

(Rev. 71, 04-09-04)

A service may be covered by a contractor if:

It is reasonable and necessary under 1862(a) (1) (A) of The Act.

Only reasonable and necessary provisions are considered part of the LCD.

Reasonable and Necessary

In order to be covered under Medicare, a service shall be reasonable and necessary. When appropriate, contractors shall describe the circumstances under which the proposed LCD for the service is considered reasonable and necessary under 1862(a) (1) (A). Contractors shall

consider a service to be reasonable and necessary if the contractor determines that the service is:

Safe and effective;

Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary); and

Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is:

- o Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;
- o Furnished in a setting appropriate to the patient's medical needs and condition;
- o Ordered and furnished by qualified personnel;
- o One that meets, but does not exceed, the patient's medical need; and
- o At least as beneficial as an existing and available medically appropriate alternative.

13.7.1 - Evidence Supporting LCDs

(Rev. 71, 04-09-04)

Contractor LCDs shall be based on the strongest evidence available. The extent and quality of supporting evidence is key to defending challenges to LCDs. The initial action in gathering evidence to support LCDs shall always be a search of published scientific literature for any available evidence pertaining to the item/service in question. In order of preference, LCDs should be based on:

Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and

General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:

- o Scientific data or research studies published in peer-reviewed medical journals;
- o Consensus of expert medical opinion (i.e., recognized authorities in the field); or
- o Medical opinion derived from consultations with medical associations or other health care experts.

Acceptance by individual health care providers, or even a limited group of health care providers, normally does not indicate general acceptance by the medical community. Testimonials indicating such limited acceptance, and limited case studies distributed by sponsors with financial interest in the outcome, are not sufficient evidence of general acceptance by the medical community. The broad range of available evidence must be considered and its quality shall be evaluated before a conclusion is reached.

The LCDs, which challenge the standard of practice in a community and specify that an item is never reasonable and necessary, shall be based on sufficient evidence to convincingly refute evidence presented in support of coverage. Less stringent evidence is needed when allowing for individual consideration or when reducing to the least costly alternative. “

Note: The concept of Least Costly Alternative is no longer in use but has not been stricken from the manual)

4. Comment

“3 Note that WPS does not propose to restrict any modalities other than proton therapy.

4 Anthony L. Zietman, “Correction: Inaccurate analysis and results in a Study of Radiation Therapy in Adenocarcinoma of the Prostate,” JAMA 299 No. 8 (2008): 898-900 and Anthony L. Zietman et al., “Comparison of Conventional-Dose vs High-Dose Conformal Radiation Therapy in Clinically Localized Adenocarcinoma of the Prostate. A Randomized Controlled Trial,” JAMA 294 No. 10 (2005): 1233-1239.

5 Allan Pollock et al., “Prostate Cancer Radiation Dose Response: Results of the M. D. Anderson Phase III Randomized Trial,” International Journal Radiation Oncology Biology Physics 53 No. 5 (2002): 1097-1105. “

Response

The assumption that WPS does not propose to restrict any modalities other than proton therapy is wrong. WPS has LCDs on radiation therapy, IMRT, stereotactic radiosurgery, brachytherapy and others. We look at these policies as an explanation of coverage. Sometimes they are restrictive but that is because the science is not adequate enough to support additional coverage.

5. Comment

Second, the draft makes no reference to the criteria used for actually making its coverage determinations. By law, Medicare coverage hinges on whether an item or service is “reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” The draft does not reference this standard or the criteria contained in section 13.5.1 of the Medicare Program Integrity Manual. Without knowing the criteria for making the specific determinations, it is not possible for interested parties to make meaningful comments or provide relevant information to WPS.

Response:

We follow all CMS guidance for our policy making decisions. We have quoted the regulations earlier. We assume from this statement that you do not wish us to follow these guidelines. i.e.

Safe and effective;

Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary); and

LCDs should be based on:

Published authoritative evidence derived from definitive randomized clinical trials or other definitive studies, and

General acceptance by the medical community (standard of practice), as supported by sound medical evidence based on:

- o Scientific data or research studies published in peer-reviewed medical journals;
- o Consensus of expert medical opinion (i.e., recognized authorities in the field); or
- o Medical opinion derived from consultations with medical associations or other health care experts.

6. Comment

Also, without a full explanation of the criteria used, it is possible that WPS may have used inappropriate criteria to evaluate proton beam therapy. The law does not authorize CMS or its contractors to deny coverage for therapies that are more expensive than therapeutic alternatives or to require that a provider demonstrate that the therapy a physician has ordered for a patient is comparatively more effective than other treatments, yet this draft LCD appears to rely on such criteria.²

It is well known that, in some cases, Medicare payment for proton therapy may be greater than alternative therapies. Although WPS has not specifically cited cost as a basis for this LCD, it has not provided any other motivation for why WPS is seeking to limit coverage of proton therapy. If WPS seeks to limit coverage for other reasons—such as whether proton therapy is safe or effective—it should explain those bases in a new draft LCD and re-issue the draft LCD for comment.

Response

We are aware that by law we cannot use the criteria of Least Costly Alternative and we do not signify this in any way in our policy.

6. Comment

Specifically, if WPS should decide to proceed with this LCD, WPS should specify the key questions that were used to guide the evaluation of the evidence to make a determination of reasonableness and medical necessity for each patient condition, and provide a detailed analysis of these questions in light of the evidence. In this analysis, WPS should explain what standard threshold of evidence it relies on to determine whether a procedure is covered in every day practice or under the auspices of a clinical trial. Although the draft LCD provides a bibliography of the literature reviewed, it fails to discuss how this literature may have been important in making the determinations of coverage. Without such information, it is not possible to comment on the application of that literature to the determinations. It also calls into question the extent to which WPS considered new or ongoing research in its work. This is especially troubling since proton therapy has an extensive literature that demonstrates its appropriateness for conditions for which the draft LCD proposes significant coverage restrictions.

Response

The policy is a draft and in that form we expect comments and additional literature be sent supporting ones coverage position. In fact that has been the case and we have received numerous comments and much literature on this topic, some for restricting and some for expanding coverage.

We do not plan to withdraw the policy. Chicago is in your consortium and we are working with physicians in that area among others on this draft. The policy on Proton Beam Therapy is

currently being reorganized and under re- review by a task force of radiation oncologists from our jurisdictions. We are allowing more time to complete it because there is no absolute consensus from the experts on coverage.

Testimonials:

We received about 80 patient testimonials on the benefits of proton therapy for prostate cancer with requests for coverage without limits. We have considered these statements in our assessment.