THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Proton Therapy

August 23, 2017

Attn: Anthem Corporate Appeals
Anthem Blue Cross Blue Shield
P.O. Box 27401
Richmond, VA 23279

RE: Dianne Weber
MDACC: [redacted]
Policy #:
Group#:
DOB:

FIRST LEVEL APPEAL: EXPEDITED/LIFE-THREATENING APPEAL

Dear Clinical Team:

This letter is a response to the Anthem Blue Cross Blue Shield adverse determination of the prescribed proton beam radiation therapy to your insured member, Mrs. Dianne Weber. I am appealing the decision on an expedited (urgent) basis and request ANTHEM BCBS approve proton beam therapy (PBT) for Mrs. Weber's life-threatening diagnosis of recurrent squamous cell carcinoma to her pelvic and intra-abdominal lymph nodes.

Please keep in mind that this should not be reviewed as a routine anal cancer case. Mrs. Weber had previous conventional radiation to her anal canal in 2012 which immediately overlaps with her current treatment site. We cannot effectively treat her recurrent cancer by administering another course of conventional photon radiation. This presents a clinical challenge due to the serious side effects following re-irradiation.

Comparative planning was performed and clearly identifies proton beam therapy as the superior modality (please see comparative planning data below).

Given the clinical complexity of Mrs. Weber's case, ANTHEM BCBS should approve this request immediately without further delay.

We request a **Specialty Match Reviewer** that is a board-certified radiation oncologist with proton beam clinical experience.

TIMELINE OF EVENTS

The urgent request for authorization was submitted on August 14, 2017. The adverse denial of service was issued August 16, 2017. Incredulously, prior to the denial, we called and were able

to schedule a peer to peer with AIM for 2pm. When our physician called, we were informed that we could not perform the peer to peer as the case was denied at 12pm. The physician protested and was allowed to speak with another physician who simply stated that it was denied and that "they did not have an indication for protons." We were instructed to appeal the decision.

CLINICAL SUMMARY

Mrs. Weber is a 58 year-old young woman with an extensive clinical history dating back to 2012. She was diagnosed with T1 squamous cell carcinoma of the anal canal and received chemoradiation in 2012. Her anal cancer was treated to 51Gy in 28 fractions. During her treatment, she developed systemic and skin toxicities that lead her to not receive her second dose of Mitomycin C and interrupted a week of her radiation treatments. She remained disease free up until 9/2016 when she started to experience pain, pressure, and cramping in her pelvic area. This gradually got worse, therefore subsequently underwent further testing including colonoscopy and scans. A PET/CT on 2/6/17 showed metabolically active confluent adenopathy at the aortic bifurcation extending right left common iliac nodes and right internal/external iliac nodes was consistent with metastatic disease. She reports sacral discomfort with prolonged sitting. She now has recurrent squamous cell carcinoma to her pelvic and intra-abdominal lymph nodes.

REASON FOR DENIAL

ANTHEM BCBS denied PBT citing that the service requested is considered experimental or investigative.

A. ANTHEM BCBS MEDICAL POLICY IS INCOMPLETE AND OUTDATED

In reviewing ANTHEM BCBS Radiation Therapy criteria, to which there are many reference articles, it is of note there are **ZERO** specifically pertaining to recurrent anal cancers. Moreover, there are **ZERO** reference articles about re-irradiation with Proton Therapy.

The National Comprehensive Cancer Network NCCN, updated 2017 guidelines are not listed in the Radiation Therapy Criteria as a current reference used for determination. This is notable because this industry recognized guideline specifically approves and details the use of Proton Beam Therapy. Additionally, the NCCN has updated the guideline 3 times this year (January, February, and June 2017) to each detail the use of Proton Therapy, and recommended it as the standard of care.

ASTRO's newly released Model Policies for PBT (July 2017) echoes the same support that PBT is medically necessary where sparing the surrounding normal tissue cannot be adequately achieved with photon-based radiotherapy and is of added clinical benefit to the patient. Mrs. Weber's cancer condition meets all **four** of the criteria below.

1. The target volume is in close proximity to one or more critical structures and a steep dose gradient outside the target must be achieved to avoid exceeding the tolerance dose to the critical structures.
2. A decrease in the amount of dose inhomogeneity in a large treatment volume is required to avoid an excessive dose "hotspot" within the treated volume to lessen the risk of excessive early or late normal tissue toxicity.
3. A photon-based technique would increase the probability of clinically meaningful normal tissue toxicity by exceeding an integral dose-based metric associated toxicity.
4. The same or an immediately adjacent area has been previously irradiated, and the dose distribution within the patient must be sculpted to avoid exceeding the cumulative tolerance dose of nearby normal tissue.

We have provided you with a list of 3 references supporting the use of proton therapy for re-irradiation, as well as 1 specifically detailing bowel involvement with re-irradiation, and additionally the current NCCN guidelines.

B. PROTON THERAPY IS REQUIRED BECAUSE OF MRS. WEBER'S HISTORY OF PREVIOUS IRRADIATION.

Mrs. Weber was previously treated to 51Gy with conventional radiation. Mrs. Weber's bowel has already received a max dose of more than 50Gy from her previous treatment. The small bowel is sensitive to radiation, with a max allowable dosing of 50Gy. The Standard of Cumulative Dosing requires a modification of a treatment plan to ensure threshold doses are not exceeded. To treat Mrs. Weber with conventional radiation would require compromising and treating a smaller area minimizing overlap and effectively not treating the tumor site with full therapeutic dose. Given her existing cumulative dose, she has significantly increased risk for subacute complications: chronic diarrhea, and radiation enteritis, strictures, abscess and fistula.

Citing the Cumulative Dose standard of care Mrs. Weber's local providers refused to treat her with conventional radiation and recommended Proton Beam Therapy at MDACC. This is a very complex treatment plan that exceeds the capabilities of most facilities. As an example, we will use deformable image registration, and digitally recreate her previous dose onto the current treatment CT for the most accurate accounting for cumulative dosing.

As outlined in "Re-Irradiation: New Frontiers" (Nieder et. al), Proton Beam Therapy is the treatment of choice and when a safe treatment alternative cannot be achieved.

> The rationale for proton re-irradiation is often to avoid or reduce toxicities of re-irradiation by limiting the volume of non-target tissues receiving additional radiation dose. In some diseases, proton re-irradiation may improve outcomes

by facilitating safe dose escalation or providing better target coverage while respecting constraints to clinical normal structures. In uncommon cases, **proton therapy may permit re-irradiation when the dosimetry achieved with other modalities is felt to preclude safe re-irradiation**. [*Emphasis added*]

As described, the proton plan will have reduced volume of *low dose* compared to IMRT. The unavoidable low dose bath created by conventional IMRT will permeate immediately adjacent structures (**bowel, soft tissue, skin, bladder, and bone marrow**) increasing toxicity creating acute and late effect reactions that will be avoided with Proton Therapy (Fig. 1). This is of great concern due to the previous irradiation. The proton plan will utilize a scanned delivery technique (IMPT) to deliver the most conformal dose possible. As demonstrated below (Fig. 2), the Proton Beam Therapy plan will have almost zero dose beyond the target as well as sharpened lateral penumbra reducing spillover onto the previous radiation site and sparing distal organs and structures.

Mrs. Weber's medical history is significant for both radiation-induced injuries and postsurgical complications. She has extensive surgical issues stemming from her previous excisions, all complicated by high dose radiation in the proximity of the current treatment site. Mrs. Weber currently suffers from radiation-induced injuries: skin toxicities, sacral pain and discomfort.

As a result, Mrs. Weber **cannot** be treated with conventional IMRT radiation without compromising previously exposed bowel, bladder, skin, bone marrow and soft tissue further complicating possible post radiation excision. Furthermore, exposing healthy bone marrow to unnecessary low dose radiation will make it very difficult for Mrs. Weber to tolerate her chemotherapy.

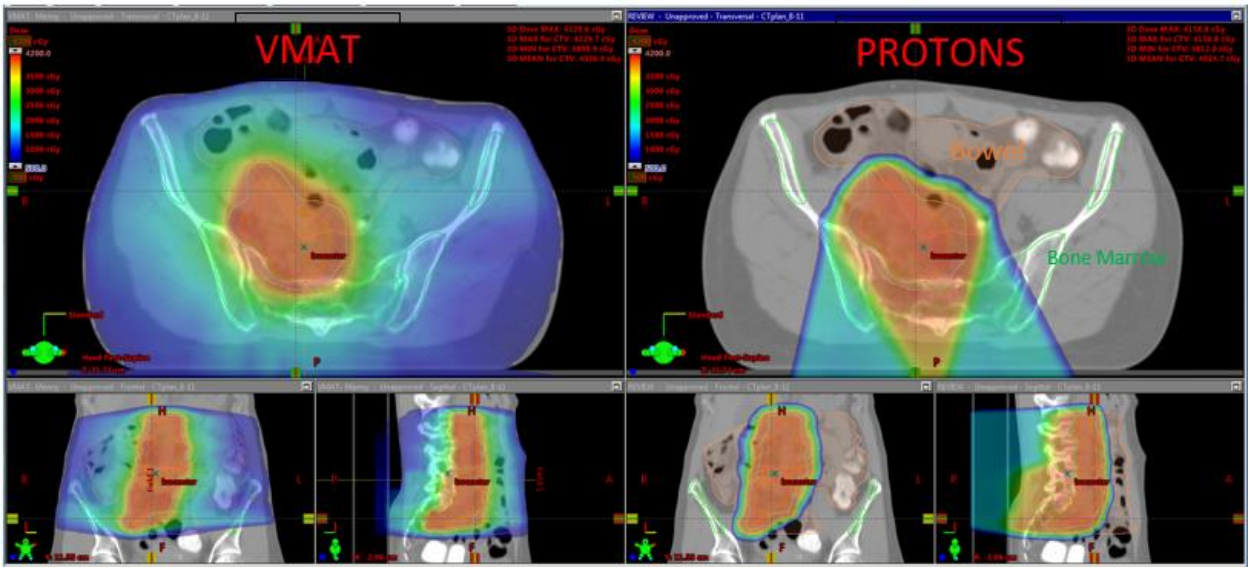

Fig 1: Mrs. Weber's proton treatment plan (right) significantly reduces radiation to her bowel, bone marrow, and skin. Proton therapy has a much lower entrance dose and no exit dose. Conventional photon based techniques would irradiate significantly larger volumes of these sensitive structures.

Pre-operative Proton Beam Therapy will deliver minimal dose distally beyond the target, sparing the small bowel, bladder, and superficial skin minimizing acute desquamation and ultimately less fibrosis.

C. TO DENY PROTON BEAM THERAPY FOR MS. WEBER'S INDICATION IS TO TREAT THIS RADIATION MODALITY DISPARATELY.

The AIM reviewing physician, and therefore, Anthem BCBS's, stated reason for denial that there is "no indication for treatment with proton beam" ignores several obvious facts. First, undisputedly, the standard of care is to treat Mrs. Weber's cancer and its subsequent recurrence with radiation therapy. Second, the use of conventional radiation and IMRT are limited given her previous irradiation (previously approved by Anthem BCBS). Third, the comparative planning confirms that proton beam radiation is superior to other forms of radiation. Taken together, the conclusion is that radiation therapy is medically necessary and that the selection of proton beam as a modality is supported by both the clinical facts and objective comparative treatment planning. To deny proton beam in the face of the standard of care treats proton beam therapy disfavorably over photon. This runs afoul of recently passed Virginia law.

Virginia **state law** states:

> *Notwithstanding the provisions of § **38.2-3419**, each policy, contract, or plan issued or provided by a carrier that provides coverage for cancer therapy shall not hold proton radiation therapy to a higher standard of clinical evidence for decisions regarding coverage under the policy, contract, or plan than is applied for decisions regarding coverage of other types of radiation therapy treatment.*

Under the state law mentioned above, to deny Mrs. Weber proton therapy, which should be treated as an equal to other types of radiation therapy treatment, is to deny Mrs. Weber radiation therapy all together.

D. PROTON BEAM THERAPY FOR REIRRADIATION IS NOT EXPERIMENTAL AND INVESTIGATIONAL

It is not reasonable or accurate to characterize proton therapy as experimental or investigational. Proton versus photon studies have been compared in many studies including re-irradiation cases

over the years. It has been proven that proton therapy causes less radiation dosage to normal tissue and surrounding structures which is why it's a better treatment choice for Mrs. Weber than other alternatives such as IMRT and 3D conformal.

Proton beam therapy minimizes toxicity for Mrs. Weber and results in a more rapid recovery from the treatment of her life-threatening recurrent squamous cell carcinoma to her pelvic and intra-abdominal lymph nodes, resulting in better outcomes, less complications and lower cost to her and you (as her insurer). Specifically, proton therapy will be an outpatient treatment and will not require hospitalizations due to her disease. Less radiation dose to surrounding tissues and critical structures will in turn decrease hospital stays and emergency room visits for Mrs. Weber due to diarrhea, bowel fistula, nutritional deficits, and skin irritation and breakdown. Furthermore, in the pre-operative setting Proton Beam Therapy will deliver less dose to surrounding soft tissue minimizing fibrosis and creating a better surgical outcome.

The evidence base supporting proton therapy's medical necessity goes back a decade. Most important, proton beam therapy is supported as evidence-based care by both the National Comprehensive Center Network's guidelines (updated three times this year) and ASTRO Model Policy (released last month).

To characterize proton therapy as experimental/investigational or unproven is to deny the standard of care for Mrs. Weber.

CONCLUSION

Mrs. Weber's treatment is complicated because she has previously been irradiated, and gone through several surgeries in the same area. Her previous radiation has compromised the integrity of her skin and soft tissue, with appearance of superficial nerve damage (increased sensitive) and fibrosis. Cumulative dosing to the impacted area will be above 90Gy requiring specialized care, monitoring and skill. After irradiation, Mrs. Weber could undergo an additional surgery to remove more lymph nodes. Mrs. Weber's previous radiation did not spare her small bowel and took it to over tolerance (50Gy); cumulative dosing to this structure must be respected.

1) Proton Beam Therapy is the superior (and the only) treatment option for local control and minimized toxicity to the small bowel, skin, and deep tissue.
2) Proton Beam Therapy offers improved survivability based on a clinically significant reduction in comorbidities that result from excessive radiation exposure. Preventing acute and late effect radiation induced complications, improving her quality of life and reduced costs by mitigating future procedures/hospitalizations.
3) Proton Beam Therapy, as demonstrated, is necessary to prevent unnecessary overlap between previous radiations.

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Given everything that Mrs. Weber has been through with her condition, we feel that this is the best option for her both from the medical and humane standpoint. We request that you overturn your decision to deny this request.

I respectfully request that you approve Mrs. Weber's Proton Therapy treatment. Again, proton therapy is FDA-approved and is not experimental and investigational and is proven in treatment of recurrent anal cancers and shown to be superior in the re-irradiation setting. Under Virginia state law you must treat proton beam therapy equally to other types of radiation therapy. We feel that ANTHEM BCBS should follow Traditional Medicare guidelines that cover proton therapy thus her proton treatment for her life-threatening recurrent anal cancer should be covered under her health plan.

Per ANTHEM BCBS's policy, a decision can be made within 72 hours for an expedited appeal. Therefore, we anticipate a response no later than August 25, 2017. We appreciate your prompt, detailed response to this request.

Should additional clinical information be required, please contact Manuel Oyervides CMD Clinical Program Manager, at 832-750-1848.

Please return/forward all correspondence to:

The University of Texas M.D. Anderson Cancer Center -
Proton Therapy Center
Attention: Manuel Oyervides CMD
1840 Old Spanish Trail
Houston, Texas 77054
Tax ID # 760679446

Sincerely,

Emma B. Holliday
Assistant Professor
Department of Radiation Oncology
The University of Texas MD Anderson Cancer Center

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Enclosures:
Scholarly Articles to Support PBT.
Clinical Information

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APPENDIX A:
REFERENCES SUPPORTING THE USE OF PROTON BEAM THERAPY FOR REIRRADIATION

Proton Beam Reirradiation for Recurrent Head and Neck Cancer: Multi-institutional Report on Feasibility and Early Outcomes. P. Romesser MD, O. Cahlon MD, E. Scher, E. Hug MD, K Sine CMD, C. DeSelm MD, J. Fox MD, D. Mah MD, M. Garg MD, J. Chang MD, N. Lee MD Int. Jour Rad Onc 5/2016

A Prospective Study of Proton Beam Reirradiation for Esophageal Cancer. A. Fernandes MD, A. Berman MD, R Mick MRS, S. Both PhD, K Lelionis MRS, J. Lukens MD, E. Ben-Josef MD, J. Plastaras MD

Proton Reirradiation of Recurrent Rectal Cancer: Dosimetric Comparison, Toxicities, and Preliminary Outcomes. A. BermanMD, S. Both PhD, T. Sharkoski, K. Goldrath, Z Tochner MD, S. Apisarnthanarax MD, J. Metz MD, J. Plastras, MD

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APPENDIX B:

NCCN VERSION 1.2017

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APPENDIX C:

ASTRO Model Policy