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Original article

Granulomatous slack skin disease: a new combined proton and photon therapy approach with a reported case response

Jonathan B. Farr[1], Allan F. Thornton[1], Avril O'Ryan-Blair[1], Chris E. Allgower[1], Arnold L. Schroeter[2], Andries N. Schreuder[1]

[1]*Midwest Proton Radiotherapy Institute (Renamed Indiana Health Proton Therapy Center in 2008), Indiana University, Bloomington, IN, USA,* [2]*Mayo Clinic, Department of Dermatology, Rochester, MN, USA*

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Abstract

Purpose: Here, we report the feasibility and long-term efficacy of a granulomatous slack skin disease (GSSD) treatment with combined high-energy photon and proton beams.

Patient and methods: A GSSD patient with abdominal disease volume $25 \times 15 \times 2$–4 cm deep was recommended for treatment at this institution. In addition to photons and electrons, high-energy protons delivered with advanced planning techniques and patient positioning were used. The patient was irradiated to a total dose of 40 Gy by using 20 Gy matched photon and electrons followed by 20 Gy equivalent protons delivered by using innovative range compensation and patient positioning.

Results: The test patient tolerated the treatment well and is now a 10-year survivor of the disease.

Conclusions: Treatment of GSSD with protons is feasible. The range and narrow penumbra properties of the proton beam provided an ideal capability to match fields accurately to cover large volumes while also sparing underlying normal tissues.

Keywords: granulomatous slack skin disease; proton therapy; robotic patient positioning

INTRODUCTION

Granulomatous slack skin disease (GSSD)

GSSD is a rare condition related to mycosis fungoides. It is characterised by the insidious development of hanging, pendulous folds of skin in flexural regions. Accordingly, histopathologic examination results reveal characteristic granulomatous infiltrates.[1–3] GSSD has recently been recognised as being a cutaneous lymphoma on the basis of findings of clonal lymphocyte populations in T-cell receptor gene rearrangement studies.[4,5] Within this lymphoma classification, GSSD and granulomatous mycosis fungoides exhibit similar histology and are differentiated solely by clinical differences, with GSSD being recognised by the presence of hanging folds of skin.[6] In addition, there exists a correlation

Correspondence to: Jonathan B. Farr, Department of Radiological Sciences, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Mail Stop 220, Memphis, TN 38105 2794, USA. Tel: + 901 595 8059. Fax: + 901 595 3981. E-mail: jonathan.farr@stjude.org

between GSSD and Hodgkin lymphoma, with GSSD patients expressing lymphoma symptoms prior or subsequently to the GSSD.[2,7,8]

Treatment with ionising radiation

There is currently no known effective long-term treatment for GSSD. Partial responses have been reported with various modalities, including topical, localised and systemic treatments used singly or conjunctively. There are only two reports of complete remissions, with the longest duration being 2·5 years.[2,9] Because the lympho-proliferative nature of GSSD has been recognised only recently, systemic chemotherapy has been used only sparingly. The focus of GSSD treatment delivery has been the use of localised methods. In the case of radiotherapy, hiatus to individual lesions in some patients has been reported,[10,11] but the paucity of long-term follow-up has prevented a determination of efficacy.

Radiative treatments typically involve skin electron beam irradiation similar to that used for localised mycosis fungoides.[12–16,11] Although such a treatment of a GSSD patient with electrons has been reported,[11] the relatively large field sizes required for these plans can be problematic because of the need for precise field matching, which is particularly difficult with electron beams. The sharp penumbrae from megavoltage (MV) photon beams make tight field matching possible, but use of the modality is accompanied by attendant irradiation of normal tissues as the beam exits the target.

Our approach was based on our thinking that developing a proton therapy approach for GSSD could offer the benefit of sharp field matching as with MV photons, but without the exit dose as with electrons. Thus, we could achieve a suitable radiative dose deposition to the neoplasm while sparing underlying tissues.

PATIENT AND METHODS

Patient

In 1997, a lesion developed on the left abdomen of a 19-year-old man after an abrasion accident involving abdominal skin. Initially considered to be a silica granuloma, the lesion was treated with topical intra-lesional steroids, ultraviolet light B phototherapy and topical ointments. In 1998, punch biopsy results indicated granulomatous inflammation having an area of $9{\cdot}5 \times 4\ cm^2$. By 2002, the affected region had progressed to $25 \times 15 \times 2$–4 cm deep and was accompanied by hypercalcaemia and renal insufficiency thought to be secondary to the granulomatous process. After referral of the case to the Mayo Clinic in 2003, a diagnosis of GSSD was given. The clinic photograph presented as Figure 1 shows the extent of disease across the patient's abdomen at that time.

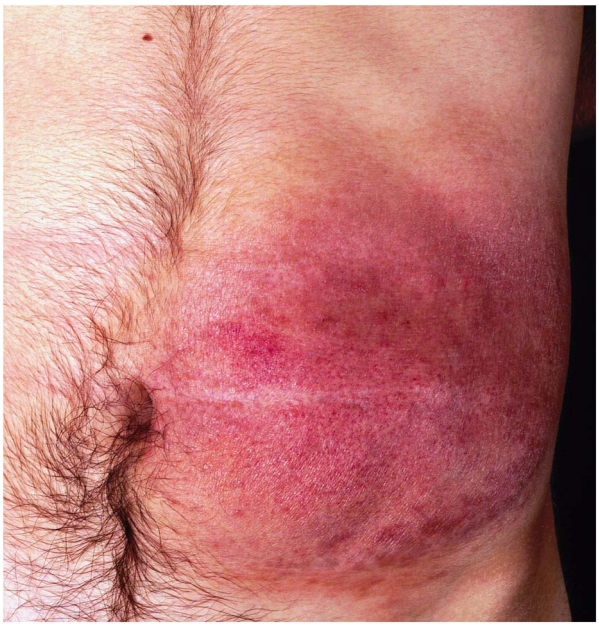

Figure 1. Detail photograph of the patient's disease in 2003.

After the GSSD diagnosis, local radiotherapy was administered to downregulate the antigenic potential of the tumour by irradiating the bulk of the disease. The use of chemotherapy was contra-indicated by its potential to harm the patient's already-compromised immune system. Because of the patient's age and renal complications, we wanted to spare underlying critical abdominal structures. Thus, the specific treatment objectives were well aligned with the potential benefit of the new proton therapy application.

Treatment facility and equipment

The proton therapy equipment available at Midwest Proton Radiotherapy Institute[i] in 2004 consisted of

[i]Renamed the Indiana University Health Proton Therapy Center in 2008.

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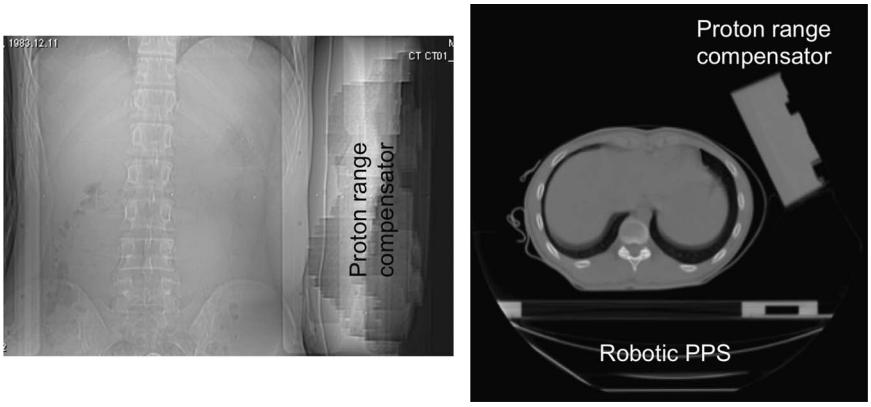

Figure 2. The treatment planning computer tomography on the left shows inclusion of the proton range compensator. After computer treatment planning, the plan was recalculated to permit mounting the range compensator into the patient's immobilisation aid (right image) for delivery. An effect of the ranged proton beam was to pull the dose delivery off the underlying parenchyma. The range compensator was required to tailor the distal end of the dose distribution to the target volume and account for the curve of the patient's abdomen. Abbreviation: PPS, patient-positioner system.

a nominal 208 MeV proton beam in a single fixed horizontal beamline (FHBL) room, with the beam using a double passive scattering system and fixed range modulator.[17–19] The beamline is similar to many other passive systems currently in clinical use.[20,21] The FHBL room takes advantage of a novel robotic patient-positioner system (PPS) that was built by an industrial robot (Motoman Model UP200, Motoman Inc., Miamisburg, OH, USA)[22] having a specified accuracy of 300μm when transiting a payload of up to 200 kg. This accuracy combined with 6 degrees of freedom provides the PPS with excellent patient-positioning capability, which is especially desirable given the angular limitation of the FHBL. The facility has since been updated to include more advanced scanning proton therapy technology.[23,24] The photon treatment capability consisted of a standard commercial medical linear accelerator with 6 MV photons and 15 MeV electrons available.

RESULTS AND DISCUSSION

Treatment plan and delivery

In addition to the angular beam delivery limitations of the FHBL room, the field size was limited at the time of treatment to a maximum diameter of 12 cm from the room's 'isocentre'. Under these conditions, four patched proton fields at extended source-to-surface distance were required to achieve the target volume coverage. This approach added the further difficulty of abutting multiple adjacent fields on a daily basis as well as uncertainty of the dosimetry of the gap junctions.

A unique solution was developed to minimise these uncertainties: by using the precision of the robotic PPS coupled with a fixed range compensator attached to the patient immobilisation device rather than to the treatment nozzle, full coverage of the intended curved, abdominal surface was obtained (Figure 2). The oversize range compensator was included as part of the patient's immobilisation, with the patient and immobilisation device positioned by the robotic PPS. The range compensator form was estimated from a preliminary plan and then built into the immobilisation. A subsequent computer tomography planning scan was obtained of the patient, immobilisation device and fixed range compensator and imported back into the treatment planning system (Computerized Medical Systems Inc., St. Louis, MO, USA: model FOCUS Radiation Treatment Planning System with Proton Planning Capability) for verification.

The representative axial gross target, photon and proton-planned doses are presented in Figure 3. The iso-dose levels most closely conform to the target volume in the proton plan, with a large degree of bowel- and kidney sparing, as depicted in the dose volume histogram (Figure 4).

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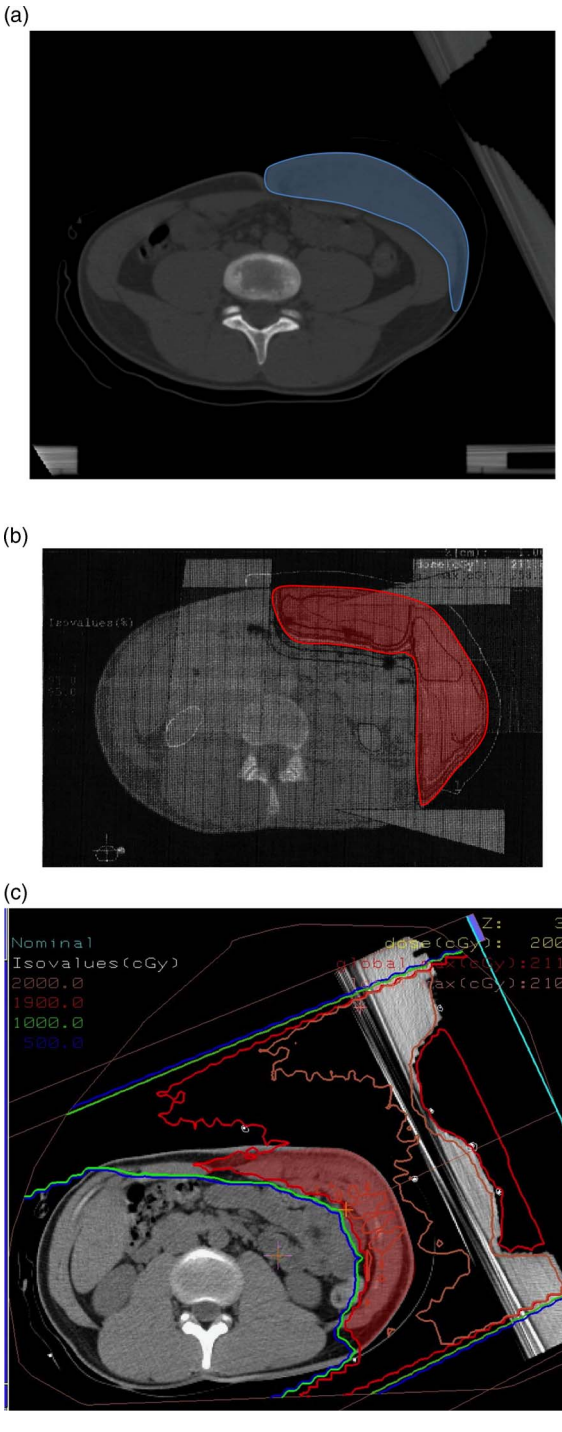

Figure 3. (a) Representative axial slice of the target volume for treatment, (b) combined 6 MV-wedged photon AP-PA and matched 15-MeV electron plan and (c) proton treatment plan. The proton treatment plan conforms optimally to the target.

The dosimetric characterisation process and verification of the treatment plan delivery is available elsewhere.[25]

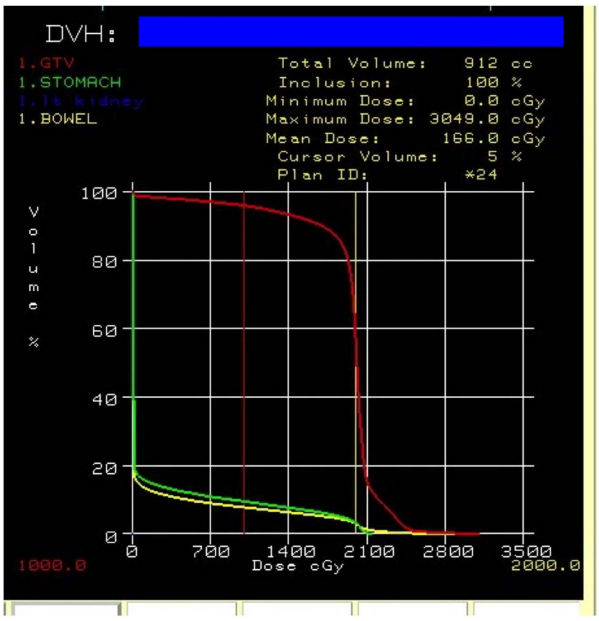

Figure 4. Proton treatment plan: dose volume histogram.

Therapeutic dose and fractionation

Because of the difficulties of the delivery in this case, the patient's treatment was initiated with X-rays and electrons while the proton plan and patient-specific devices were being developed. The total treatment went to a total dose of 40 Gy, composed of 20 Gy delivered with 6 MV AP-PA to a $6{\cdot}7 \times 24$ cm^2 region and 20 Gy delivered to the adjacent 20×20 cm^2 region with 15 MeV electrons in ten fractions. The treatment was then completed with an additional 20 Gy (60-Co equivalent[26]) protons to a custom 25×15 cm^2 field in ten fractions.

Patient outcome

Ten years post treatment, the patient has an excellent outcome, has completed university studies and works professionally. This result compares favourably with published outcome data.[2,6] On this basis, we believe that either this new technique consisting of combined photon and proton therapy or a proton-only approach should be studied further for GSSD patients.

CONCLUSIONS

The first hybrid photon/particle treatment approach for GSSD has now been developed and delivered to a patient. The treatment technique in this particular

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case was tailored to overcome a series of technical difficulties. By using the precision of a robotic PPS, coupled with a fixed range compensator attached to the patient immobilisation device rather than to the treatment nozzle, full coverage of the intended curved abdominal surface was obtained with a high degree of conformity. The range and narrow penumbra properties of the proton beam provided an ideal capability to match fields accurately to cover large volumes while sparing underlying normal tissues. The patient tolerated the treatment well and is a 10-year survivor of the disease. Because definitive therapy for GSSD is not yet established, we have sought to provide an example of using radiotherapy to provide adequate treatment for GSSD while concurrently reducing concomitant dose volume to surrounding tissues.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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