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Celebrating Our True Colors

John H. Suh, MD, FASTRO, FACR

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As the year draws to a close, it is common for many of us to reflect on the relationships that shape the ebb and flow of our daily lives, especially at home and in the workplace. Both a congested store overflowing with anxious holiday shoppers and a busy and complex radiation oncology department are reliable case studies for evaluating a range of human behaviors, especially in response to stress.

On either stage, emotional intelligence—with domains in self-awareness, self-management, social awareness, and relationship management—plays an integral role in how we behave, influencing many factors such as interpersonal relationships and professional burnout. In this month's *Applied Radiation Oncology*, the authors of *Personality Mapping and Emotional Intelligence Education in Radiation Oncology* demonstrate how the True Colors framework can be used within the workplace to cultivate emotional intelligence and team awareness. Implementation of the tool in the radiation oncology department of their comprehensive cancer center facilitated department-wide discussions on communication preferences and interpersonal styles, which build and maintain relationships.

The initiative not only enhanced awareness of emotional intelligence but also influenced departmental structure, including the creation of a new leadership role. Such work reinforces that high-quality cancer care is built upon both technical precision and the human competencies that sustain collaboration.

In *Using an Auto-planned VMAT-TBI Technique for Myeloablative Autologous HSCT for Scleroderma*, Hui et al demonstrate how automated VMAT-TBI was able to meet stringent organ-sparing requirements in the STAT-2 trial while reducing toxicities and eliminating the practical burdens of conventional block-based techniques. Their work illustrates the growing feasibility of highly conformal, script-based TBI planning, even within the narrow therapeutic window required for patients with scleroderma.

A similarly patient-centered focus characterizes *Treatment of Stage IIB Seminoma in a Patient with Down Syndrome with Eisenmenger Syndrome: A Case Report*, which highlights the complexity of balancing oncologic efficacy with cardiopulmonary risk in a population rarely represented in clinical trials. The authors demonstrate that conventional-dose dog-leg radiation therapy can achieve a complete response with minimal toxicity in a patient for whom chemotherapy posed unacceptable risk. Beyond its clinical relevance, the case reminds us that radiation therapy can be the safest curative modality when systemic options are limited.

From individualized case management to population-level prognostication, the study *Impact of Integrated Pathologic Score on Treatment Outcomes for Borderline Resectable Pancreatic Cancer* evaluates the IPSCAP score in patients treated with neoadjuvant chemotherapy and 5-fraction SBRT followed by resection. IPSCAP proved a robust predictor of overall survival across chemotherapy regimens, with lower scores correlating strongly with improved outcomes. Notably, patients receiving ≥45 Gy SBRT were more likely to achieve favorable pathologic responses. These findings highlight the promise of composite, post-treatment scoring systems to better stratify risk and refine future treatment strategies in a disease historically marked by therapeutic resistance.

As always, I thank you for being part of the *Applied Radiation Oncology* community. We wish you a joyful holiday season and a New Year filled with peace, hope, health, and continued learning!

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RESEARCH ARTICLE

Using an Auto-Planned VMAT-TBI Technique for Myeloablative Autologous Hematopoietic Stem Cell Transplantation for Scleroderma (The STAT-2 Trial)

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Abstract

Objectives The STAT-2 trial mandates lung and kidney sparing to 25% of the prescription dose and image guidance for kidney localization, posing challenges for institutions using conventional two-dimensional (2D) Total body irradiation (TBI) techniques. This study demonstrates implementation of an auto-planned volumetric modulated arc therapy-total body irradiation (VMAT-TBI) technique to facilitate STAT-2 patient enrollment and improve dissemination of modern TBI.

Materials/Methods Our institution clinically implemented and automated VMAT-TBI treatment planning, and adapted scripts to meet STAT-2 trial requirements. Three patients were treated with 3-isocenter VMAT plans in head-first supine position and 2-isocenter anteroposterior and posteroanterior plans in feet-first supine position. A custom rotational platform facilitated patient orientation changes. Cone-Beam Computed Tomography provided image guidance for lung and kidney localization. Dosimetric indices for lungs and kidneys were retrospectively reviewed for three patients. Point doses were recorded at the head, neck, shoulder, mid-mediastinum, lumbar spine, hip, knee, and ankle to confirm dose uniformity.

Results For a prescription dose of 8 Gy in 4 fractions, the average point doses for lungs and kidneys were 1.9±0.2 Gy and 1.9±0.4 Gy, respectively. Lungs_eval and kidney D_{mean} were 2.6±0.1 Gy and 2.9±0.5 Gy, respectively. Eight anatomical dose points throughout the body met the prescription criteria within ±10% consistent with the trial constraint. The treatment was well tolerated with minor post-treatment toxicities (G1 diarrhea, G2 nausea, and G1 mucositis).

Conclusions Average lung and kidney point dose constraints were achieved for the three patients. Dose–Volume Histogram metrics were achieved on average within 0.60 Gy for lungs_eval and 0.90 Gy for kidney volumes. VMAT-TBI offers superior treatment delivery for scleroderma patients, eliminating the need for heavy physical blocks and complexity of kidney localization. Auto-planning scripts are freely available on GitHub for wider VMAT-TBI adoption.

Keywords: TBI, total body irradiation, VMAT-TBI, scleroderma

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Introduction

Total body irradiation (TBI) is an important component in conditioning regimens for patients undergoing hematopoietic stem cell transplantation (HSCT). Depending on the type of transplantation, TBI may serve different purposes, such as suppressing the recipient's immune system or killing the existing marrow cells to prevent graft rejection. However, the treatment-related risks of TBI can be significant, highlighting the need to develop techniques to mitigate treatment sequelae.

Modern radiation techniques to deliver TBI show promising advantages over current methods, including improvements in dose calculation accuracy, significant reductions in dose to organs at risk (OAR), and decreased patient toxicities.[1-3] However, widespread implementation of these techniques has been hindered by the increased complexity of treatment planning and delivery. Conventional two-dimensional (2D) TBI involves placing the patient far from the radiation source at distances greater than 4 meters. The simplicity of planning and treatment for this technique has led to its dominance in TBI. However, multi-isocenter conformal arc therapy techniques such as volumetric modulated arc therapy (VMAT) and TomoTherapy provide attractive alternatives, especially when individualized OAR sparing must be prioritized.[4]

TBI is used to treat autoimmune diseases such as scleroderma, which is characterized by abnormally increased collagen synthesis and fibrosis that affects the skin, with variable involvement of the joints, lungs, heart, digestive tract, and kidneys. Conventional therapies involve immunosuppressive drugs; however, TBI followed by autologous HSCT has demonstrated significant clinical improvements in multiple trials.[5-7] Despite these benefits, radiation therapy must be used with caution in these patients, owing to concerns for increased treatment-induced fibrosis.[8-10] As a result, the TBI scleroderma trials mandated significant sparing of the lungs and kidneys to an upper limit of 2 Gray (Gy) for a prescription dose of 8 Gy (SCOT, STAT trials).[11,12] Challenges in meeting these constraints have been reported in the literature[13]; therefore, the purpose of this study was to evaluate the feasibility of adhering to them in the context of volumetric modulated arc therapy-Total body irradiation (VMAT-TBI).

Methods

Patient Cohort

This institutional review board-approved single-institution retrospective study focused on three patients who received VMAT-TBI from 2019 to 2023, who were also enrolled in the STAT-2 trial. Data collected from patient medical records and included demographics, disease characteristics, treatment details, outcomes, and follow-up.

VMAT-TBI Procedure

The VMAT-TBI technique used in this study has been described in detail in our previous publications,[2,14-16] and only a brief summary will be provided here. Full-body CT scans were acquired with a Siemens Biograph PET-CT scanner using 5 mm slice thickness. Patients were simulated on a custom rotational couch top ("Spinning Manny") attached to the CT couch top. For these patients, two sets of plans were created owing to the limitations of the longitudinal travel extent of the treatment couch: VMAT plans with the patient positioned in the head-first supine position, and additional anteroposterior and posteroanterior (AP/PA) plans with the patient positioned in the feet-first supine position. The target was defined as the entire body contracted by 0.3 cm, subtracting lungs with a 0.5 cm isotropic margin and kidneys with a 0.5 cm margin medially; a 2.0 cm margin anteriorly/posteriorly and superiorly/inferiorly; and a 2.5 cm margin laterally. Plans were normalized such that the 90% planning target volume (PTV) body was covered by the prescription dose. Dosimetric planning objectives were based on STAT-2 recommendations, where lungs_eval and kidney volumes receive a mean dose (D_{mean} ≤25% of the prescription dose), and the dose to the anatomical points is within 10% of the prescription dose. The anatomic points as defined by the trial were reference points distributed along the patient's longitudinal axis (head, neck, shoulder, mid-mediastinum, lumbar spine, hip, knee, and ankle), as well as central points within the right lung and right kidney blocks. Each point was specified in the protocol as being located midway between the entrance and exit points of the opposed radiation beams of conventional TBI.

According to the STAT-2 trial recommendations, "If [lungs] shielding is done with MLCs, the above [lung block] edges shall be used for the lung contours, and optimization will be used to limit the mean lung dose to 200 cGy." We interpreted this to mean that the lung_eval volume should receive less than 25% of the prescription dose. We followed the guidelines for lung blocks from the trial: "The lateral edges should be 1.0-1.5 cm from the inner border of the ribs, the inferior edges should be 1.0-1.5 cm from the dome of the apex of the diaphragm, 1.0-1.5 cm below the clavicles and the medial border, and 2.0-2.5 cm from the lateral edges of the thoracic vertebral bodies, with contouring to incorporate the hilae in the field." Lung_eval volume was created using the block specifications above and was used for dosimetric evaluation of dose to lungs. From the trial text: "Right Lung ("Point 9"): This reference point is defined in the center of the right lung block. The point is taken to be midway between the entrance and exit points of the opposed radiation beams." Accordingly, we evaluated the lung point dose at the mid-lung anterior-posterior separation and at the mid-lung superior-inferior extent. Similarly, the STAT-2 trial recommends kidney volume sparing to 25% of the prescription dose. In 2020, the planning process was automated due to the time-consuming nature of these

cases, and the STAT trial volumes and constraints were incorporated into the automated scripts.[14,15]

As presented in our previous works,[14,15] the auto-planning scripts automate many of the tedious and time-consuming tasks required for treatment planning in these cases; these include optimization structure, target, and plan creation, as well as isocenter/beam and isocenter placement. Furthermore, the optimization process was automated for performance of multiple successive optimizations without planner intervention. In addition, the developed software was made to be open source on GitHub to enable other clinics to adopt autoplanning into their own practice (https://github.com/esimiele/VMAT-TBI-CSI). All patient cases reported in this work were autoplanned using these scripts. Intensity-modulated radiation therapy quality assurance was performed using electronic portal imaging device portal dosimetry for each VMAT field with gamma criteria of 3%/2 mm with a 10% dose threshold. Gamma analysis, as first proposed by Low et al,[17] is routinely used in radiation oncology to compare measured and calculated two-dimensional dose distributions that consider deviations in dose and distance domains where "gamma criteria" specify the maximum acceptable deviations in each domain. The magnitude of the deviation at every measurement point is calculated; if it falls within the ellipse created by the gamma criteria, the point is considered to pass (i.e., the deviation is acceptable), whereas a point outside of the ellipse fails. In addition, in vivo dosimetry using optically stimulated luminescence dosimeters was performed at the matchline between the VMAT and AP/PA portions of the patient's treatment plan.

Toxicities

Toxicity data were identified by reviewing each patient's weekly visit notes, their hospital admission notes during the peri-transplant period, and records from subsequent follow-up visits with the stem cell transplantation team. Acute toxicities were graded using Common Terminology Criteria for Adverse Events version 5.[18]

Results

Patient Characteristics

Three patients were identified and included in the analysis as shown in **Table 1**. All three were female, and their ages at the time of radiation treatment were 34, 50, and 56 years. The median follow-up time was 46 months (range 20-64 months). The mean height and maximum width across patients were 162.1±4.5 cm and 49.7±5.3 cm, respectively.

Treatment Characteristics and Dosimetry

Treatment for each patient utilized five isocenters: head, chest, pelvis, upper legs, and lower legs. The dose prescribed was 8 Gy to be delivered in four fractions twice daily. In our cohort, the average mean dose was 2.6±0.1 Gy for the lung_eval (2.57 Gy, 2.74 Gy, and 2.90 Gy for each patient, respectively) and 2.9±0.5 Gy for the kidneys (3.36 Gy, 2.92 Gy, and 2.39 Gy for each patient, respectively). The average point dose measurements for the right and left lungs were 1.8±0.1 Gy and 2.1±0.3 Gy, respectively. For the right and left kidneys, the mean point dose measurements were 1.9±0.4 Gy each. The average plan D1cc (dose received by 1 cc of volume) was 126±3% (**Table 1**).

All three patient plans achieved 90% coverage of the PTV with 100% of the prescription dose. A sample plan dose distribution of a patient is shown in **Figure 1**.

Toxicities

At the time of last follow-up (median 17.8 months, range 9.4-23.8 months), none of these patients experienced primary or secondary graft failure. There were no incidences of nephrotoxicity or pulmonary toxicity. Two patients experienced grade two toxicities (nausea), and no patient experienced any grade 3-5 toxicities.

Discussion

This single-institution report of three patients supports the feasibility of using VMAT-TBI to meet STAT-2 trial requirements. The STAT-2 trial mandates lung and kidney sparing to 25% of the prescription dose, and the average point dose values achieved for lungs and kidneys in our patients were 1.9±0.2 Gy and 1.9±0.4 Gy, respectively. Not only did VMAT-TBI eliminate the need for heavy physical blocks and circumvent the complexity of kidney localization associated with conventional 2D TBI treatment, but the treatment was also well tolerated with no incidences of grade 3+ toxicities, graft failure, or graft-versus-host disease.

Historically, investigators have reported a higher incidence of acute and/or late toxicities in cancer patients with autoimmune diseases receiving radiation therapy,[8,9,19-24] leading to the cautionary use of radiation therapy in patients with scleroderma. A meta-analysis published in 2002 of 15 studies of patients with nonmalignant systemic diseases such as collagen vascular disease found high incidences of grade three or higher acute and late toxicities of 12.4-70% and 7-100%, respectively. The authors concluded that patients with collagen vascular disease have reduced radiation tolerance.[19] However, the majority of recently published studies show no increased risk for acute or late toxicities in patients with collagen vascular disease,[20,25] which may be due in part to modern radiation treatment techniques. The recent CONTRAD meta-analysis of 18 studies, 10 of which included patients with collagen vascular disease, found a modest 10-15% risk of any grade 3+ toxicities, suggesting that collagen

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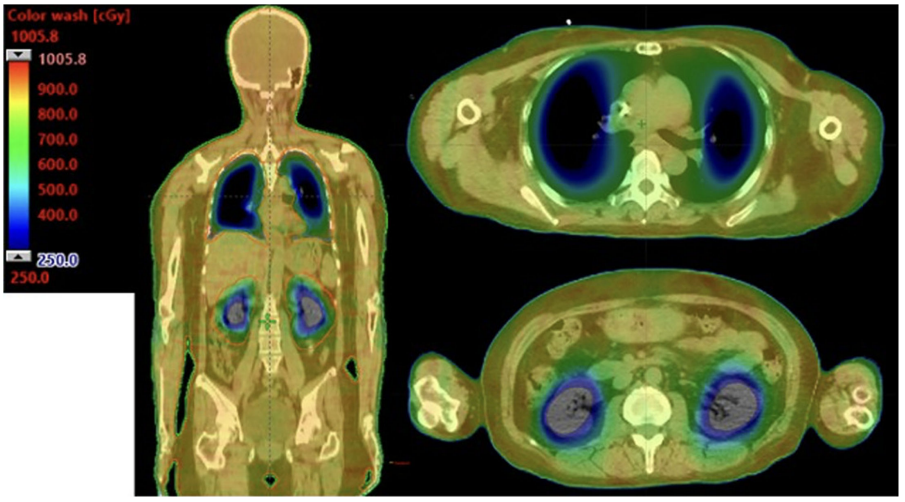
Table 1. Summary of the Dosimetric Evaluation of the Three Patients in the STAT-2 Trial Who Received VMAT-TBI Treatment

PATIENT METRICS	MIN	MAX	AVERAGE	σ
Patient height (cm)	158.6	167.1	162.1	4.5
Patient max width (cm)	44.5	55.1	49.7	5.3
Number of plan isocenters	5	5	5	0
PTV D90% (%)	100	100	100	0
PTV D1cc (%)	123	128	126	3
Lung R point dose (Gy)	1.7	1.8	1.8	0.1
Lung L point dose (Gy)	1.7	2.4	2.1	0.3
Lungs_eval D_{mean} (Gy)	2.6	2.7	2.6	0.1
Kidney L point dose (Gy)	1.5	2.3	1.9	0.4
Kidney R point dose (Gy)	1.6	2.4	1.9	0.4
Kidneys D_{mean} (Gy)	2.4	3.4	2.9	0.2

Figure 1. Coronal slices and axial slices from a patient demonstrating the dose distribution implemented in the STAT-2 trial using the VMAT-TBI technique. The visualization of the dose cloud is thresholded to 30% of the prescribed dose (2.5 Gy).



vascular disease is not an absolute contraindication to radiation therapy, as previously reported.[22]

A landmark randomized controlled trial by Sullivan et al reported improved overall survival with TBI compared to cyclophosphamide, albeit at the cost of increased toxicity to the kidneys and lungs. That study found treatment-related mortality in the transplant group of 3% at 54 months and 6% at 72 months, compared with 0% in the cyclophosphamide group.[7] Collectively, the published data support the use of radiation therapy in cases of severe scleroderma, with the caveat of adopting a cautionary approach to minimize toxicities.

In contrast to the Sullivan et al trial, the SCOT, STAT, and STAT-2 trials mandate significant sparing of the lungs and kidneys with a dose restriction of ≤2 Gy for a prescription of 8 Gy.[7,11,12] Although the strict kidney and lung dose criteria were formed to minimize radiation treatment toxicities in this patient population, recent studies have called into question the feasibility of achieving these constraints. Chiang et al performed a treatment planning study in which a validated 18 MV beam model was used to evaluate the resulting dose distribution from conventional AP/PA TBI with varying Cerrobend half-value layers (HVL).[13] The SCOT protocol specifies block edges 1-1.5 cm from a lateral chest wall, clavicle, and diaphragm dome, and a 2-2.5 cm block margin from the lateral edge of the vertebral bodies, and for the blocks to be "2 HVLs thick" to achieve a lung dose of 2 Gy. Using these guidelines, the average central point dose under the lung block exceeded the mandated 2 Gy, and it was found that the 2 Gy lung dose could not be met, regardless of block thickness (owing to scatter from the blocks).

The requirement for kidney doses was more achievable, with three HVLs meeting a renal dose requirement of 2 Gy. However, the authors pointed out the impracticality of this approach, as three HVLs of kidney and lung blocks mounted on a plastic block tray can easily exceed 18 kg (40 lbs). In addition, Craciunescu et al highlighted the challenges in renal shielding mandated by the SCOT trial owing to the difficulty of localizing the kidneys in the standing position, and they describe methods to optimize renal shielding for conventional TBI techniques with a focus on plan robustness.[26] Craciunescu et al measured average lung and kidney doses of 27.4% and 25.4%, respectively, based on extrapolated in vivo point dose measurements of 11 patients treated at their institution. However, as highlighted by Chiang et al, there can be significant differences between point dose measurements and mean organ doses depending on where the point dose is measured. Other studies have also noted discrepancies between measured, hand-calculated, and treatment-planning system-calculated doses for conventional TBI treatment techniques.[27-29] Overall, these studies conclude there is considerable ambiguity in lung and kidney dose modulation for the 2D TBI techniques and recommend that future investigators develop more

achievable, reproducible, and accurate TBI methodology.

In 2020, our institution clinically implemented multi-isocentric VMAT-TBI as an alternative to conventional TBI utilizing AP/PA beams. Although ongoing studies are investigating whether there are significant benefits of VMAT-TBI over conventional techniques, VMAT-TBI has improved dose calculation accuracy and the potential to overcome the impracticality of using multiple HVL Cerrobend blocks that achieve only sub-par dose sparing. Furthermore, VMAT-TBI has been shown to provide better OAR sparing,[2,14-16] offering a significant advantage for cases that require stringent dosimetry control levels. The reduced doses to OARs have translated to reduced toxicities. Hui et al reported a matched-pair single-institution retrospective analysis of 200 patients treated with TBI at our institution from 2014 to 2023.[3] The VMAT-TBI cohort experienced significantly lower rates of any grade of pneumonitis (2% vs 12%), nephrotoxicity (7% vs 34%), nausea (68% vs 81%), skin (16% vs 35%), and graft-versus-host disease (42% vs 62%) compared to the 2D TBI cohort. For patients undergoing myeloablative regimens, rates of pneumonitis (0% vs 17%) and nephrotoxicity (9% vs 36%) were significantly lower with VMAT-TBI versus 2D-TBI. Similar outcomes were observed in the City of Hope study by Ladbury et al.[1] Finally, Shinde et al reported pulmonary, renal, thyroid, and cataract toxicities from a prospective trial monitoring patients up to 8 years after TMI.[30] Mean organ doses were lung 7.0 Gy, kidneys 7.1 Gy, thyroid 6.7 Gy, and lens 2.8 Gy. The crude incidence of radiation pneumonitis was 0.7% and no radiation-induced renal toxicity was noted.

These studies suggest VMAT-TBI offers improved organ sparing when compared to matched or historical cohorts treated with conventional TBI, which is paramount in this high-risk patient population. The key limitation of our study is the small number of patients. Thus, no meaningful conclusions should be drawn regarding the superiority of VMAT-TBI over conventional TBI techniques. The primary objective was to assess the feasibility of achieving the rigorous STAT-2 trial dose constraints for the kidneys and lungs using VMAT-TBI, which was successfully demonstrated in this study. Overall, this work demonstrates the feasibility of an automated solution for planning and treating patients on the STAT-2 trial. It also underscores the clinical relevance of VMAT-TBI by eliminating the need for Cerrobend blocks and their associated challenges; reducing toxicities by improving dose to OAR; enabling treatment for patients who cannot tolerate prolonged standing during conventional TBI; and providing open-source automated planning scripts that facilitate reproducibility and adoption across centers. Continued adaptation of our VMAT-TBI script to additional patients with the SCOT regimen will be necessary to validate our technique in this patient population and may lead to more explicit, reproducible, and accurate TBI methodology for future trials.

Conclusions

This study presents a promising advancement in TBI techniques with the potential to significantly influence patient treatment within the STAT-2 trial. The VMAT-TBI technique offers image guidance for accurate treatment delivery, uses MLCs for lung and kidney blocking that disposes of heavy Cerrobend blocks, and expands treatment to patients who cannot tolerate standing for the prolonged duration of conventional TBI treatment. The patients in this series have experienced mild toxicities with the automated VMAT-TBI method, underscoring its effectiveness and tolerability.

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RESEARCH ARTICLE

Impact of Integrated Pathologic Score on Treatment Outcomes for Borderline Resectable Pancreatic Cancer

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Abstract

Objective The Integrated Pathologic Score of the College of American Pathologists (IPSCAP) grading system independently predicts overall survival (OS) in patients with resected pancreatic adenocarcinoma after non-ablative neoadjuvant therapy. This study analyzes the impact of IPSCAP on the outcomes of patients with borderline resectable pancreatic cancer (BRPC) resected after neoadjuvant chemotherapy and 5-fraction stereotactic body radiation therapy (SBRT).

Materials and Methods This Institutional Review Board-approved retrospective study queried patients with BRPC treated between 2013 and 2023 with either neoadjuvant FOLFIRINOX or gemcitabine-abraxane and SBRT, who underwent resection. SBRT was categorized at ablative dose thresholds of ≥40 or 45 Gy. The IPSCAP score was calculated by summing tumor regression grade, pathologic tumor stage, and nodal status for patients with more than 12 lymph nodes examined and was classified into 3 groups: group 1 (score 0-3), group 2 (score 4-6), and group 3 (score 7-8). The presence of actionable somatic and germline mutations was identified. OS was defined as the time from biopsy to death or last contact (in months). Statistical analyses were performed using R software.

Results Overall, per-unit decrease of IPSCAP was significantly associated with increased median OS (hazard ratio [HR] = 0.770, 95% CI 0.670-0.886, $P < .001$). Kaplan-Meier survival analysis showed a significant difference between stratification of IPSCAP by group, with group 1 having significantly less risk of death than groups 2 and 3. Similar results were found when patients were stratified by their neoadjuvant chemotherapy: FOLFIRINOX (HR = 0.742, 95% CI 0.604-0.912, $P < .01$) and gemcitabine-abraxane (HR = 0.804, 95% CI 0.667-0.969, $P = .022$). Patients treated with ≥45 Gy were significantly more likely to have group 1 pathologic scores and had higher odds of achieving group 1 compared with those treated with <45 Gy (odds ratio, 2.458; 95% CI 1.060-5.783; $P = .027$, Fisher exact test).

Conclusions This study suggests that IPSCAP incorporation is a reliable prognosticator in the setting of neoadjuvant chemotherapy and 5-fraction SBRT of OS in patients with resected pancreatic adenocarcinoma, warranting further studies with dose escalation in this population.

Keywords: stereotactic body radiation therapy, borderline resectable pancreatic cancer, FOLFIRINOX, gemcitabine-abraxane, IPSCAP, pathologic score

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, characterized by late presentation, early metastatic spread, and poor 5-year survival rates.[1] Within this spectrum, borderline resectable pancreatic cancer (BRPC) defined by anatomic criteria represents a challenging subset. The contact of these tumors with nearby vasculature complicates the potential for their complete surgical resection.[1,2] Neoadjuvant therapy (NAT), including chemotherapy and radiation strategies such as conventional fractionation, hypofractionation, and ablative radiation, has been used to improve resectability and long-term outcomes.

Neoadjuvant approaches have become an increasingly accepted standard in the management of BRPC. NAT aims to downstage tumors, treat micrometastatic disease early, and increase the chances of R0 resection, ultimately offering outcomes similar to those seen in initially resectable disease.[1] By initiating therapy prior to surgery, clinicians can also assess tumor biology and treatment response, which helps refine patient selection for resection.

NAT plays a critical role in improving local tumor control by reducing tumor burden and sterilizing margins near vascular structures. Multiple studies have demonstrated improved overall survival (OS) with NAT compared with upfront surgery.[3,4] Notably, concerns about increased complication rates or reduced resectability with NAT have not been substantiated, as surgical outcomes appear similar between the 2 approaches.[3] As NAT usage becomes more prevalent, the need for accurate post-treatment prognostic tools has become increasingly important. Clinical staging systems like the American Joint Committee for Cancer (AJCC) classification, which are based on untreated tumor characteristics, are less effective in predicting outcomes than the AJCC pathologic staging system, which has been validated using data from treatment-naïve patients.[5,6] In the setting of NAT, however, the optimal staging and prognostication systems remain unclear.

To address this limitation, a more dynamic prognostic system that reflects NAT response is needed. The Integrated Pathologic Score of the College of American Pathologists (IPSCAP), developed to fill this gap, was first mentioned by Sohn et al in the setting of NAT integrating nonablative radiation.[6] IPSCAP is a combination staging score following NAT and subsequent resection in patients with BRPC. Pathologic tumor stage (ypT), nodal status (ypN), and histologic tumor regression grade (TRG) are added into a single composite score, with a lower IPSCAP score representing a better pathologic outcome.[6] This score offers a more nuanced and informed measure of patient prognosis than traditional staging. Sohn et al reported IPSCAP outperformed AJCC pathologic staging (0, IA, IB, IIA, IIB, III, and IV) in predicting critical oncologic outcomes such as disease-free survival and OS. In addition, IPSCAP correlated with several key prognostic factors, including tumor differentiation, margin status, and recurrence risk.[6] In multivariate analyses, both IPSCAP and related models (IPSMDA using the MD Anderson histopathologic response grading system) have emerged as independent predictors of survival, whereas pathologic AJCC staging alone lacks more detailed prognostic insight following NAT.[6-8] These findings support IPSCAP's growing role in post-treatment evaluation and its potential as a preferred tool for guiding ongoing clinical decision-making.

With the incorporation of advanced treatment modalities, such as ablative radiation therapy, including stereotactic body radiation therapy (SBRT) and hypofractionated regimens incorporating high-dose intensity-modulated radiation therapy, the addition of radiation to NAT is becoming increasingly effective at achieving local control.[9,10] Doses of 40 to 50 Gy or more (72-100 biologically equivalent dose [BED]) delivered in 5 fractions are considered within the ablative range for PDAC.[11,12] These regimens may enhance margin sterilization, particularly when paired with systemic therapy, and could further improve patient outcomes. Currently, the role of radiation as part of NAT for BRPC is controversial, and the optimal dose/fractionation strategy is unknown.[13] This uncertainty has been reinforced by the negative findings of the Alliance trial, which established chemotherapy alone as an acceptable standard of care.[14]

By integrating key post-treatment data, IPSCAP in the setting of NAT may offer a clearer prognostication based on post-treatment tumor biology and improve adjuvant therapy patient selection. Since studies to date have not evaluated the impact of IPSCAP in NAT regimens integrating ablative radiation dosing, this study aims to further understand IPSCAP as a prognosticator of outcomes in patients with BRPC following neoadjuvant chemotherapy plus 5-fraction SBRT with subsequent resection.

Materials and Methods

An Institutional Review Board-approved retrospective study utilizing an institutional database was queried for patients with the diagnosis of BRPC treated with neoadjuvant chemotherapy and radiation. Eligible patients were treated with neoadjuvant FOLFIRINOX or gemcitabine-abraxane plus 5-fraction SBRT with subsequent resection between 2013 and 2023. Radiation therapy was administered in a single academic institution by gastrointestinal (GI) site-specific radiation oncologists using either conventional or MRI-guided linac. In the first 6 years of the study period, the departmental protocol consisted of delivering up to 40 Gy in 5 fractions to the gross tumor volume (GTV) after endoscopic placement of fiducial markers within the tumor, contingent on normal tissue constraints, as previously described.[15-17] Respiratory motion techniques using abdominal

compression or respiratory gating were standard, pending patient tolerance and effectiveness. In March 2019, our institution began our MRI linac program, delivering gated nonadaptive treatments for the first 4 months and then transitioning to gated adaptive technique once training proficiency was achieved.[18-20] With MRI adaptive capability, real-time coverage of the GTV daily could be optimized while maintaining organ-at-risk (OAR) dose constraints. This was not possible with conventional linac treatment, in which daily GTV coverage was not directly assessed.

Chemotherapy cycles were determined by physician preference. Patients with full treatment and tumor characteristic data, and at least 12 nodes examined per the College of American Pathologists minimum criteria, were included.[21] Patient data collected included demographics, CA19-9 marker and secretor status, chemotherapy information, radiation dosing, radiation modality, tumor pathology characteristics, germline and somatic actionable mutations, and median OS. Survival time was calculated as time from biopsy to date of death or last known contact. Actionable mutations included BRCA1, BRCA2, KRAS, ATM, PALB2, and HER2. CA-19-9 nonsecretor status was defined as ≤ 2 u/mL pre- and post-NAT.[22]

IPSCAP was calculated by adding the ypT, ypN, and TRG scores to yield a value from 0 to 8. The IPSCAP score was then subclassified into 3 groups for additional analysis: group 1 (0-3), group 2 (4-6), and group 3 (7-8). Kaplan-Meier survival curves were obtained. Cox regression was performed to determine OS hazard ratios (HRs) using IPSCAP as a per-unit measurement and proportionally compared with group 1 as reference. Cox regression was again performed using group 2 as reference in order to compare group 2 and group 3. This was performed overall and stratified by neoadjuvant chemotherapy selection. Patients were also stratified by dose at or above 40 Gy and at or above 45 Gy. Kaplan-Meier survival curves and Cox regression were performed to determine OS impact using dose threshold as a categorical measurement. Post-hoc chi-square testing (without Yates correction) and Fisher testing was performed comparing dose threshold to group 1 status. Analytics were performed using R software. **Tables 1 and 2** were then created based on patient and tumor characteristics overall and stratified by IPSCAP group, respectively. Median values were utilized for reporting table statistics.

Results

Results yielded 146 eligible patients treated according to our study parameters, with 71 (48.6%) patients treated with FOLFIRINOX and 75 (51.4%) treated with gemcitabine-abraxane. The median age in our cohort was 68, with a similar distribution in males vs females (see **Table 1**). A minority of patients achieved a complete pathologic response (2.7%), as well as a pathologic nonresponse (13.7%). The median OS for this cohort was 33 months, with a 2- and 3-year survival rate of 66.4% and 45.2%, respectively.

Overall, per-unit decrease of IPSCAP was significantly associated with increased median OS (HR = 0.770, 95% CI 0.670-0.886, $P < .001$). Kaplan-Meier survival curve analysis showed a significant difference between stratification of IPSCAP by groups (**Figure 1**). Using group 1 as reference, groups 2 and 3 had very significant increased risk of death (HR = 2.718, 95% CI 1.508-4.898, $P < .001$) and (HR = 4.654, 95% CI 1.916-11.307, $P < .001$), respectively. Group 3 had a higher risk of death than group 2, but it was not significant (HR = 1.713, 95% CI 0.823-3.564, $P = .150$).

When analysis was performed only on patients receiving neoadjuvant FOLFIRINOX and SBRT, decreased IPSCAP was significantly associated with increased median OS (HR = 0.742, 95% CI 0.604-0.912, $P < .01$), with a significant survival curve (**Figure 2**). Group 2 had a significantly higher risk of death compared with group 1 (HR = 5.883, 95% CI 2.056-16.830, $P = .001$) and group 3 did not (HR = 4.528, 95% CI 0.821-24.980, $P = .083$). Group 3 had a lower risk of death than group 2, but it was not significant (HR = 0.770, 95% CI 0.177-3.340, $P = .727$).

When the analysis was restricted to patients who received neoadjuvant gemcitabine-abraxane and SBRT, a lower IPSCAP score was significantly associated with increased median OS (HR = 0.804, 95% CI 0.667-0.969, $P = .022$) with a significant survival curve (**Figure 3**). Patients in group 3 had a significantly higher risk of death compared with those in group 1 (HR = 3.718, 95% CI 1.286-10.745, $P = .015$), whereas group 2 did not differ significantly from group 1 (HR = 1.654, 95% CI 0.806-3.396, $P = .170$). Group 3 had a higher risk than group 2, but it was not significant (HR = 2.248, 95% CI 0.931-5.429, $P = .072$).

When the combined cohort was stratified by dose threshold, patients receiving ≥40 Gy had an insignificant difference in OS (HR = 0.881, 95% CI 0.564-1.377, $P = .579$), with insignificant survival curves (**Figure 4**). There was also no significant association between ≥40 Gy and group 1 status (chi-square = 0.031, $df = 1$, $P = .859$; Fisher exact $P = 1.000$). Patients receiving ≥45 Gy had an insignificant difference in OS (HR = 1.064, 95% CI 0.684-1.654, $P = .784$), with a nonsignificant survival curve (**Figure 5**). However, patients treated with ≥45 Gy were significantly more likely to have group 1 status postoperatively (chi-square = 5.412, $df = 1$, $P = .020$) and had higher odds of achieving group 1 compared with <45 Gy (OR = 2.458, 95% CI 1.060-5.783, Fisher exact $P = .027$).

Within the tumor characteristics, there was a smaller proportion of patients with lymphovascular invasion when treated with ≥45 Gy; however, it was not significantly different than <45 Gy (chi-square = 2.638, $P = .104$, Fisher $P =$

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Table 1. Demographic Patient Data and Characteristics of Treatment, Tumor, and Median Overall Survival

CHARACTERISTIC	N = 146
Age	68 (33-86)
Gender	
Female	52.7% (77)
Male	47.3% (69)
Radiation dose (Gy)	
<40	24% (35)
≥40	76% (111)
<45	62.3% (91)
≥45	37.7% (55)
Radiation modality and dose	
Conventional SBRT	61.6% (90)
Adaptive MRI	37.7% (55)
MRI SBRT	0.7% (1)
Neoadjuvant chemotherapy	
Number of cycles overall	4 (1-12)
FOLFIRINOX	71 (48.6%)
Gemcitabine-abraxane	75 (51.4%)
Tumor location	
Head/neck	81.5% (119)
Body/tail	18.5% (27)
CA19-9	6 N/A
Secretor	93.6% (131)
Pre-chemo (u/mL)	160.8 (1.2-16,600)
Pre-surgery (u/mL)	27.5 (0-800.9)
% decrease	78.9% (−3291.7% to 100%)
Non-secretor	6.4% (9)
TRG	
Grade 0	2.7% (4)
Grade 1	24% (35)
Grade 2	59.6% (87)
Grade 3	13.7% (20)
Perineural invasion	
Present	74% (108)
Not identified	24% (35)
Unknown	2% (3)
Lymphovascular invasion	
Present	47.3% (69)

.113). Increased proportions of actionable somatic mutations and non-secretor status were noted as the IPSCAP group decreased (**Tables 1 and 2**). Additional patient and tumor characteristics are summarized in **Tables 1 and 2**.

Discussion

The optimal strategy for improving outcomes of patients with BRPC remains unknown and controversial. Meta-analysis has shown comparable OS outcomes between gemcitabine-based regimens and FOLFIRINOX as NAT in appropriately selected patients.[23] Conflicting Alliance data show benefit of some NAT regimens incorporating CRT while no benefit with hypofractionation or low-dose SBRT.[14,24] Studies incorporating advanced radiation technologies such as MRI-guided SBRT delivering 50 Gy in 5 fractions have included resected patients with BRPC, reporting low rates of toxicity and encouraging 2-year survival.[25]

We previously reported our own experience with 26 resected patients who received ablative SBRT (median dose 50 Gy in 5 fractions) with no perioperative deaths in 90 days and an R0 rate of 96%.[19] Our median progression-free survival from diagnosis was 13.2 months and median OS was not reached. The median time from the end of SBRT to resection was 50 days. Although the median dose translated to a BED of 100 Gy, the rate of postsurgical complications did not differ with historical controls, with an 8% rate of grade 1 pancreas anastomotic leak, grade 1 and 2 chyle leaks, grade 4 hemorrhage, and grade 2 wound infections. The rate of retroperitoneal abscess and grade 3 wound infection was 4%. In addition, the rate of postsurgical hospitalization did not differ from expected norms at our institution, with a median of 7 days. Thus, in our institutional experience, we have not observed

Table 1. continued

CHARACTERISTIC	N = 146
Not identified	45.2% (66)
Unknown	7.5% (11)
Invasion by dose	
<40 Gy	
Perineural invasion	
Present	77.1% (27)
Not identified	22.9% (8)
Unknown	-
Lymphovascular invasion	
Present	46.8% (17)
Not identified	45.7% (16)
Unknown	5.7% (2)
≥40 Gy	
Perineural invasion	
Present	73% (81)
Not identified	24.3% (27)
Unknown	2.7% (3)
Lymphovascular invasion	
Present	46.8% (52)
Not identified	45% (50)
Unknown	8.1% (9)
<45 Gy	
Perineural invasion	
Present	75.8% (69)
Not identified	23.1% (21)
Unknown	1.1% (1)
Lymphovascular invasion	
Present	52.7% (48)
Not identified	40.7% (37)
Unknown	6.6% (6)
≥45 Gy	
Perineural invasion	
Present	70.9% (39)
Not identified	25.5% (14)
Unknown	3.6% (2)
Lymphovascular invasion	
Present	38.2% (21)
Not identified	52.7% (29)

increased perioperative complications after resection with ablative dose.

Although the desired outcome of treatment for patients with BRPC is prioritized as R0 resection, our IPSCAP data reveal improved pathologic outcomes, with lower scores suggesting a potential role for optimizing response strategies by including SBRT. Similar studies to this one on neoadjuvant treatment strategy for BRPC have been noted in the literature. Leung et al showed better local recurrence-free survival in patients treated with SBRT and chemotherapy vs chemotherapy alone. Patients included in the SBRT group had more advanced baseline disease yet achieved significantly better post-treatment pathologic T stage, N stage, and perineural invasion, with similar OS.[9] Results from Hill et al showed chemotherapy plus SBRT had no difference on OS vs chemotherapy alone but did have increased node negative, pathologic complete response, and negative margin resections in patients with locally advanced and BRPC.[26] Zakem et al showed TRG 0 and 1 combined showed significantly increased OS (41 mo) compared with TRG 2 (25 mo) and 3 (24 mo).[27]

Based on the results of the present study, IPSCAP has validity as a robust postoperative multimodal pathology metric, and a very strong predictor of OS in patients treated with NAT incorporating 5-fraction ablative SBRT. Per-unit IPSCAP decrease is associated with a 23% decreased chance of death in patients with BRPC treated with neoadjuvant chemotherapy and 5-fraction SBRT prior to resection. In addition, this study's results provided insight into the differences in pathologic outcomes stratified by FOLFIRINOX and gemcitabine-abraxane. FOLFIRINOX shows a superior survival with outcomes compared with gemcitabine-abraxane (HR = 0.742 vs HR = 0.804). Interestingly, our analysis also noted

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Table 1. continued

CHARACTERISTIC	N = 146
Unknown	9.1% (5)
Overall combined survival	33 (6-140)
2-y OS	66.4% (97)
3-y OS	45.2% (66)
Survival by radiation dose (Gy)	
<40	31 (13-114)
≥40	33 (8-140)
<45	37 (6-140)
≥45	29 (10-70)

Abbreviations: OS, overall survival; SBRT, stereotactic body radiation therapy; TRG, tumor regression grade.

increasing proportions of actionable somatic mutations and non-secretors in lower IPSCAP groups. A similar study evaluating patients treated with chemotherapy and SBRT showed significantly better pathologic tumor regression grades in patients with KRAS mutations.[28] Not all patients in our cohort received germline and somatic mutation testing, which limits comprehensive understanding of these impacts given that our study parameters included patients treated before routine institutional testing. Further studies incorporating these mutations into multivariate analysis may reveal the influence of genetic mutation status on IPSCAP and OS.

Our study raises significant questions about the correlation of ablative dose with IPSCAP. Our analysis shows that there is an increased achievement of lower IPSCAP group 1 in doses at or above 45 Gy. However, there is no OS benefit in this cohort. Doses of ≥45 Gy were only achievable in our department with the integration of the adaptive MRI linac technology, and only 37.7% of the patients included in this study received such treatment. With the MRI plans, we had daily confirmation of the GTV coverage and had the adaptive capability to optimize coverage if OAR tolerances were maintained. In addition, shortly after we instituted the MRI linac program, Hill et al published their data on the locoregional failure patterns in resected patients and advocated for including a generous clinical target volume (CTV).[29] Accordingly, our GI Radiation Oncology physician group adopted this change in practice, routinely incorporating larger CTV volumes for treatment on the MRI linac. Thus, during the 10 years of this institutional experience, there was significant heterogeneity in the volume of GTV coverage to the prescribed dose, as well as the volume of the treatment field. Further prospective studies are needed to evaluate the question as to how ablative dose/volume escalation affects clinical outcomes for patients with BRPC, especially with the incorporation of uniform volumetric contouring as per the recent NRG consensus guidelines so that rigorous quality assurance can be maintained.[10] Such studies should also carefully evaluate the contribution of dose to perioperative morbidity and toxicity, which was beyond the scope of this present 146 patient analysis. Future trials should integrate IPSCAP as a metric in order to further validate outcomes and serve as a valuable prognosticator for clinicians to measure patient response to treatment and evaluate higher-risk patients for tailored adjuvant therapies.

Limitations

This study was retrospective and conducted over a 10-year period reflecting differences in institutional treatment technology and contouring volumes that affected the prescribed dose. Lower doses were generally delivered before the incorporation of the MRI linear accelerator at our institution. As the study was retrospective in nature, it represents a heterogeneous patient population that may affect outcomes. Median OS calculations inherently include numbers that are derived from last contact, possibly lowering the reported median OS on more recent patients who may be still alive. Larger doses (ie, ≥45 Gy) were incorporated in this series with the integration of MRI-guided SBRT at our institution; thus, Kaplan-Meier and Cox regression are more reliable sources of OS interpretation vs median OS noted in the tables. In addition, low n values in group 3 may limit true interpretation of hazard risk among groups. GTV coverage to prescription dose increased with the MRI linac adaptive treatment capability due to real-time normal tissue accounting. This may positively influence postoperative pathology; therefore, the interpretation of dose impact on postoperative pathology should be considered. One patient had <2 u/mL CA-19-9 pre-treatment and 40.7 post-treatment and was labeled as a secretor.

Conclusion

Whether 5-fraction SBRT in addition to systemic chemotherapy improves the treatment outcomes of patients with BRPC is unclear at this time. Further prospective preoperative studies are needed to evaluate the impact of treatment-specific SBRT factors such as dose/volume escalation on clinical outcomes. This study suggests that IPSCAP incorporation is a reliable prognosticator in this setting and may be able to define high-risk patient populations that would benefit from tailored adjuvant therapies.

Table 2. Tumor and Treatment Characteristics Stratified by the Integrated Pathologic Score of the College of American Pathologists Group

CHARACTERISTICS (RANGE OR COUNT)	GROUP 1 (N = 35)	GROUP 2 (N = 103)	GROUP 3 (N = 8)
Age	69 (34-86)	68 (33-81)	70 (55-82)
Gender			
Female	60% (21)	50.5% (52)	50% (4)
Male	40% (14)	49.5% (51)	50% (4)
Tumor location			
Head/neck	71.4% (25)	86.7% (89)	62.5% (5)
Body/tail	28.6% (10)	13.6% (14)	37.5% (3)
CA19-9	1 N/A	*4* N/A	1 N/A
Secretor	91.2% (31)	93.9% (93)	100% (7)
Pre-chemo (u/mL)	111.1 (6.8–16600)	176.9 (1.2–15287.1)	288.9 (16.8-535.6)
Pre-surgery (u/mL)	16 (0–342.2)	32.5 (0-800.9)	68.6 (25-214.8)
% decrease	83.4% (−16% to 100%)	79.4% (−3291.7% to 100%)	60% (−122% to 91.4%)
Non-secretor	8.8% (3)	6.1% (6)	-
Perineural invasion			
Present	45.7% (16)	81.5% (84)	100% (8)
Not identified	51.4% (18)	16.5% (17)	-
Unknown/indeterminate	2.9% (1)	2% (2)	-
Lymphovascular invasion			
Present	14.3% (5)	55.4% (57)	87.5% (7)
Not identified	77.1% (27)	36.9% (38)	12.5% (1)
Unknown/indeterminate	8.6% (3)	7.7% (8)	-
Radiation dose 40 (% of group)			
<40 Gy	22.9% (8)	23.3% (24)	37.5% (3)
>40 Gy	77.1% (27)	76.7% (79)	62.5% (5)
Radiation dose 40 (% of group)			
<45 Gy	45.7% (16)	70% (69)	75% (6)
>45 Gy	54.3% (19)	30% (34)	25% (2)
Mutations (% of # tested)			
Germline tested	−23	−56	−2
Actionable mutation	13% (3)	19.6% (11)	–
No actionable mutation	87% (20)	80.4% (45)	100% (2)
Somatic tested	−7	−41	−5
Actionable mutation	85.7% (6)	70.7% (29)	60% (3)
No actionable mutation	14.3% (1)	29.3% (12)	40% (2)
Combined OS	45 (10-136)	30 (6-140)	25.6 (15-65)
Survival by radiation dose			

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Table 2. continued

CHARACTERISTICS (RANGE OR COUNT)	GROUP 1 (N = 35)	GROUP 2 (N = 103)	GROUP 3 (N = 8)
<40 Gy combined OS	49 (13-88)	29 (6-114)	21 (21-31)
>40 Gy combined OS	45 (10-136)	30 (8-140)	30 (15-65)
<45 Gy combined OS	53.5 (10-136)	37 (6-140)	26 (15-65)
>45 Gy combined OS	40 (18-70)	21 (10-57)	25 (20-30)

Abbreviation: OS, overall survival.

Figure 1. Kaplan-Meier survival curve comparing overall survival (OS) (months) between group 1 (Integrated Pathologic Score of the College of American Pathologists [IPSCAP] score 0-3), group 2 (4-6), and group 3 (7-8).

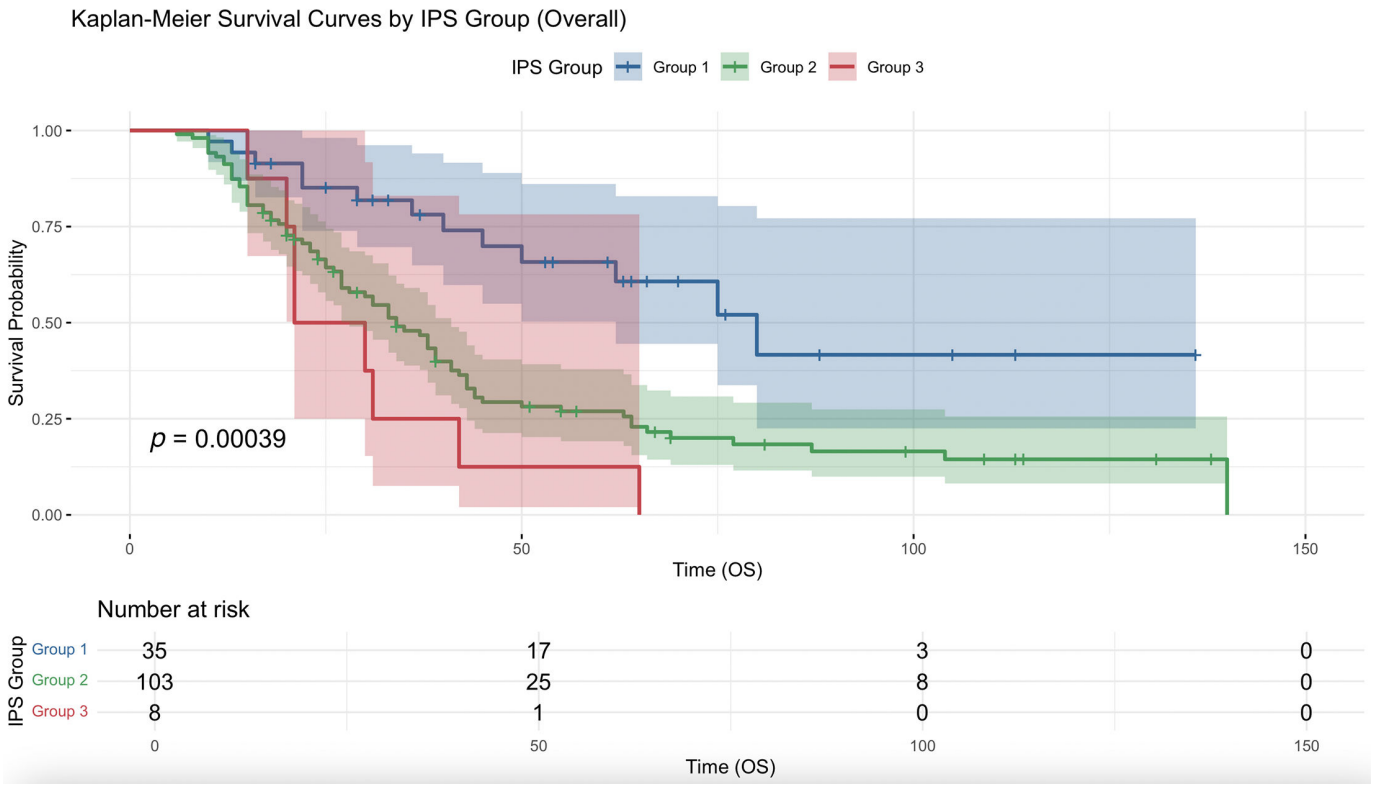

Figure 2. Kaplan-Meier survival curve for comparing overall survival (OS) (months) with neoadjuvant FOLFIRINOX and stereotactic body radiation therapy between group 1 (Integrated Pathologic Score of the College of American Pathologists [IPSCAP] score 0-3), group 2 (4-6), and group 3 (7-8).

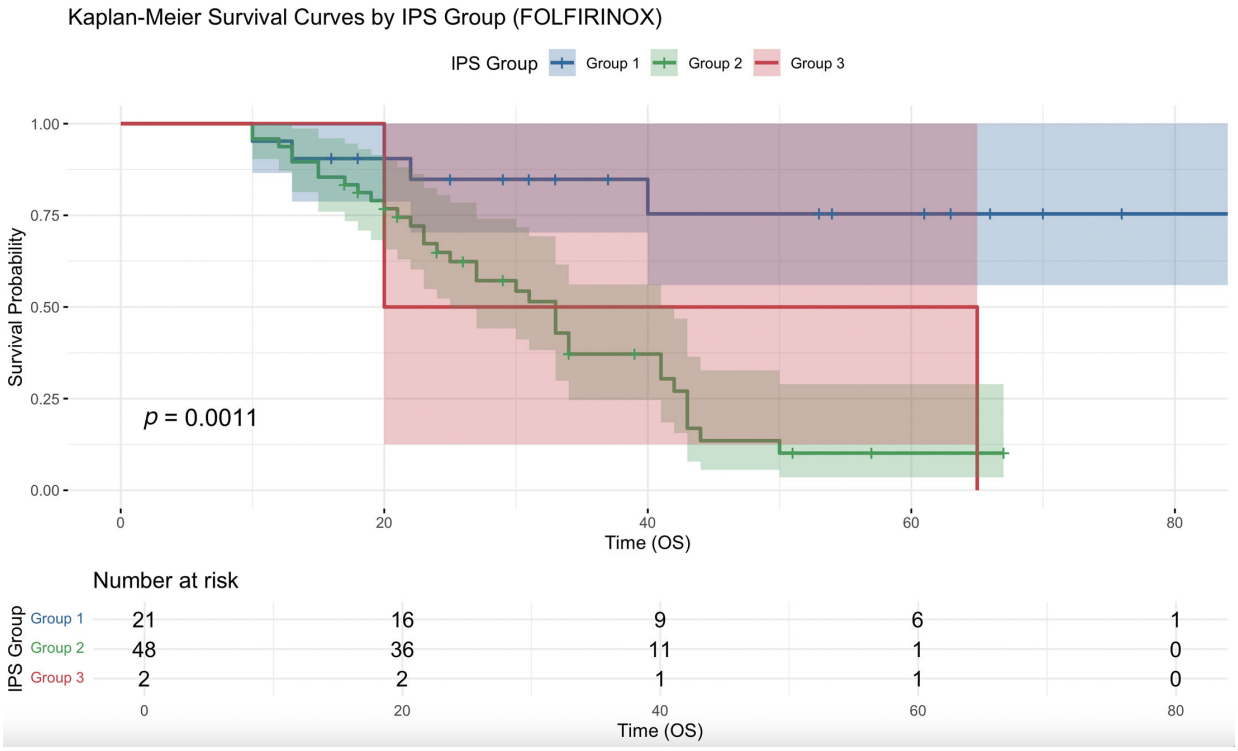

Figure 3. Kaplan-Meier survival curve for comparing overall survival (OS) (months) with neoadjuvant gemcitabine-abraxane and stereotactic body radiation therapy between group 1 (Integrated Pathologic Score of the College of American Pathologists [IPSCAP] score 0-3), group 2 (4-6), and group 3 (7-8).

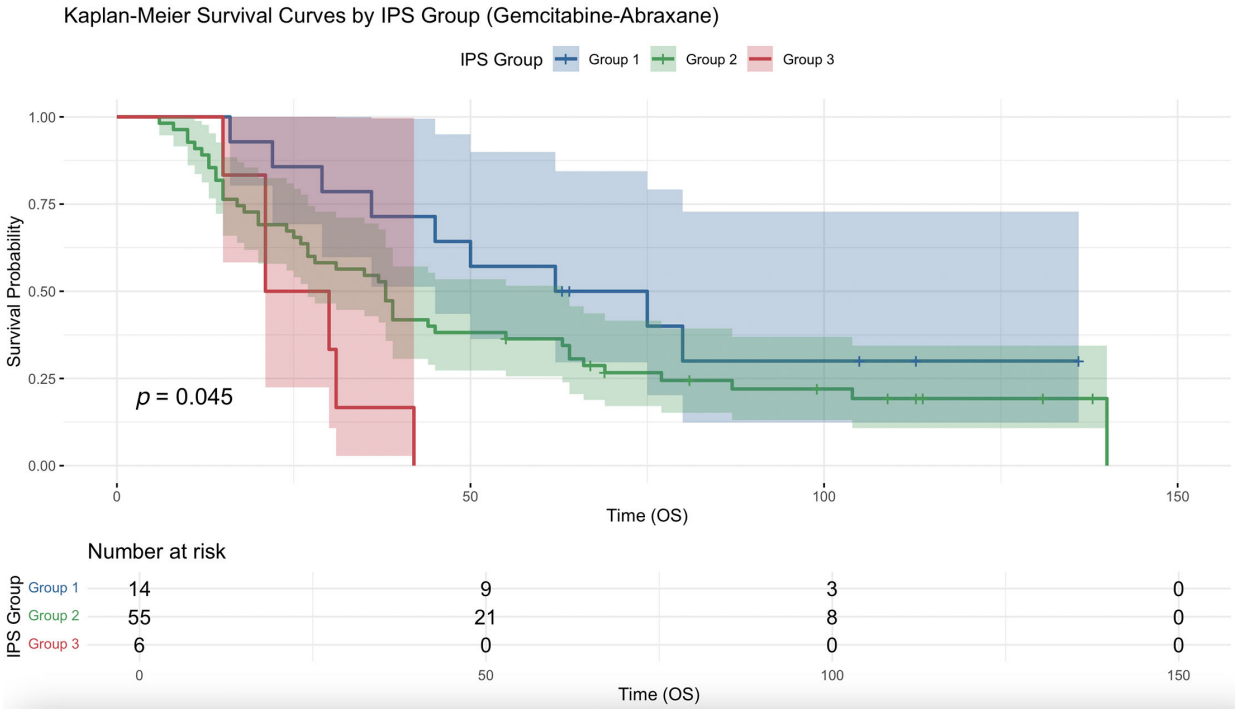

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Figure 4. Kaplan-Meier survival curve comparing overall survival (months) between ≥40 and <40 Gy.

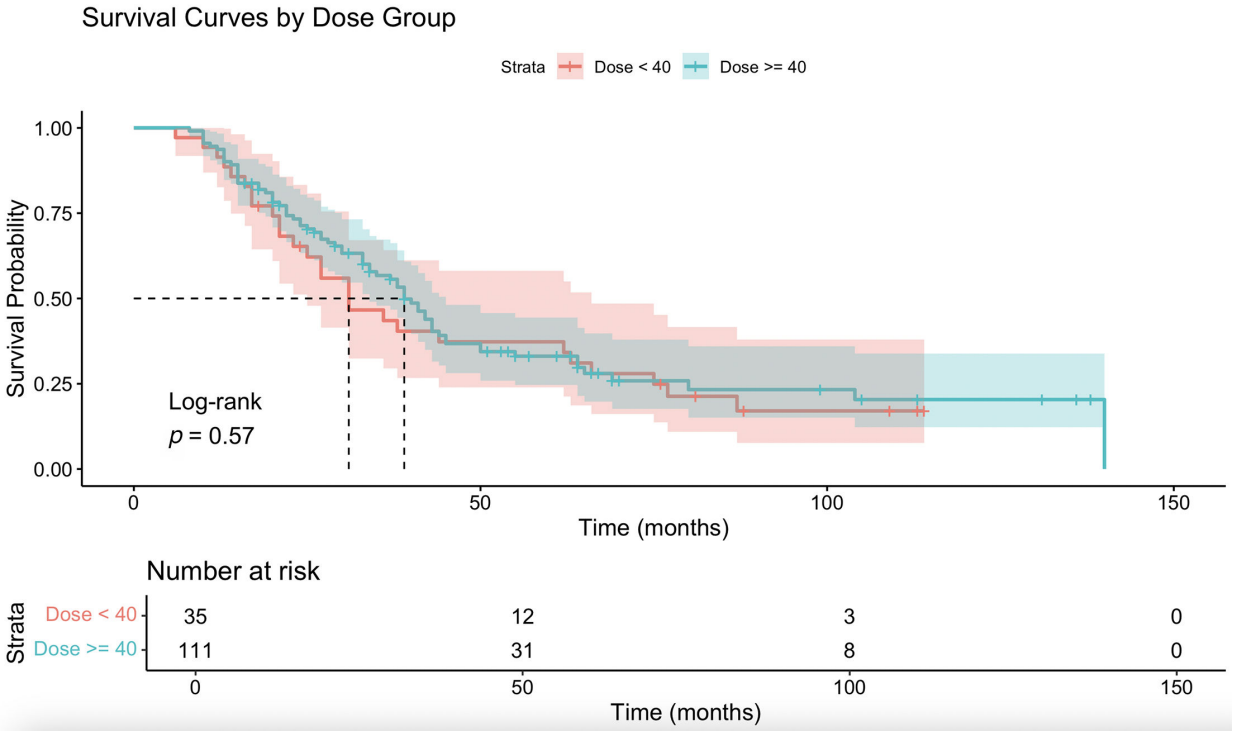
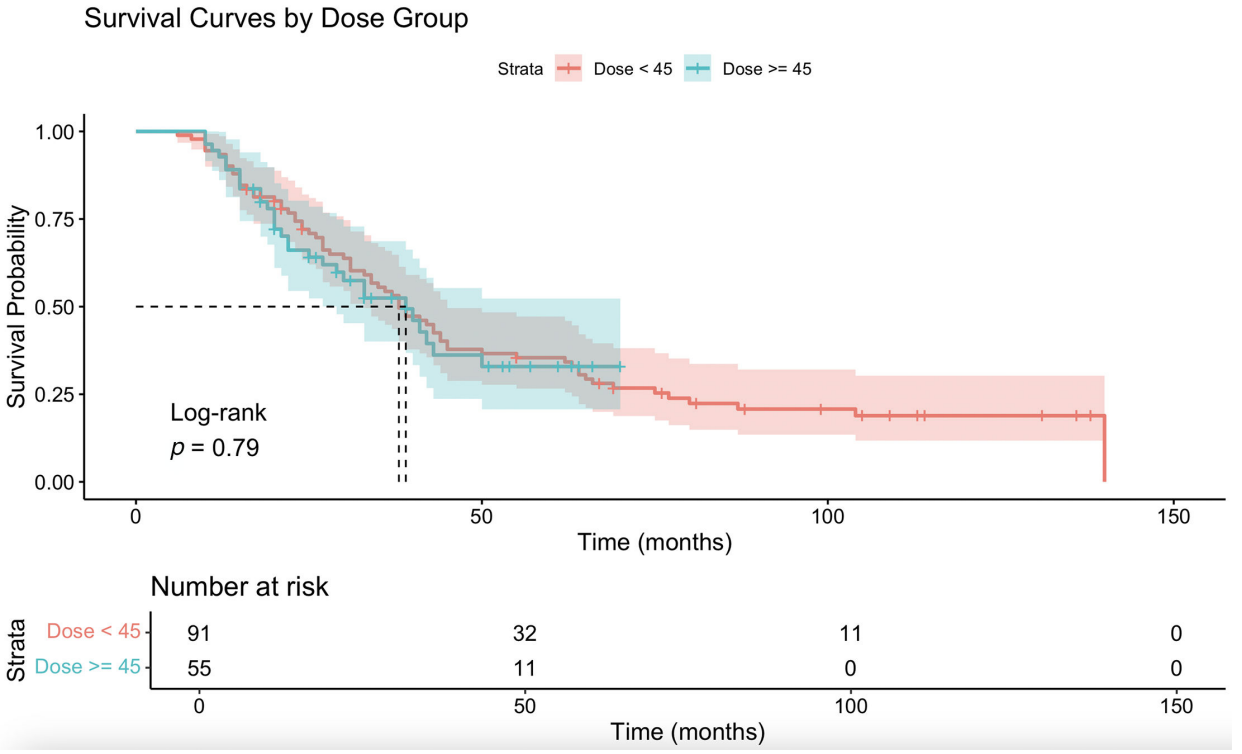


Figure 5. Kaplan-Meier survival curve comparing overall survival (months) between ≥45 and <45 Gy.



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RESEARCH ARTICLE

Personality Mapping and Emotional Intelligence Education in Radiation Oncology

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Abstract

Objectives: Emotional intelligence is essential for effective interprofessional collaboration, particularly in complex clinical settings like radiation oncology. Personality reflection tools may enhance team communication and social awareness. This study explored the distribution of personality profiles across professional roles within a radiation oncology department using the True Colors framework as part of an educational initiative.

Methods: A department-wide voluntary survey using the True Colors assessment was distributed to all staff. Participants self-identified their primary and secondary personality colors. A total of 152 responses were received from attendings (n = 14), residents (n = 14), nurses (n = 22), advanced practice providers (APPs) (n = 5), physicists (n = 15), therapists (n = 36), dosimetrists (n = 12), scheduling coordinators (n = 11), research coordinators (n = 11), research assistants (n = 2), social workers (n = 2), and administrators (n = 8). Aggregated results were presented at a town hall focused on interpersonal dynamics.

Results: Gold was the most common primary color in patient-facing roles such as nurses, attendings, and scheduling coordinators. Green was more frequently identified by physicists, APPs, and research staff. These trends were used to initiate discussions on communication preferences and emotional intelligence. Results were integrated into the residency leadership curriculum.

Conclusions: While the True Colors framework is not a validated psychometric instrument, its use as a reflective tool may help promote social awareness and team understanding in cancer education environments. These preliminary findings suggest a potential role for personality mapping in supporting emotional intelligence-based leadership training.

Keywords: emotional intelligence, professional development, teaming, personality mapping, true colors, interprofessional communication, radiation oncology resident leadership training, leadership education, relationship management

Introduction

Emotional intelligence (EI) has become a central pillar in leadership training and medical education, particularly in high-stakes environments such as oncology.[1-3] The ability to recognize, understand, and manage one's own emotions, as well as those of others, supports more effective communication, collaboration, and leadership in interprofessional teams.[4,5] These

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skills are particularly vital in radiation oncology, where successful care delivery requires tight coordination across multiple disciplines, including physicians, therapists, physicists, advanced practice providers (APPs), and administrative staff.[6,7] Indeed, in such complex multidisciplinary work environments, conflicts are anticipated and need to be effectively resolved to mitigate negative impacts such as the generation of medical errors, increased stress leading to burnout, and staff turnover. Central to many conflict scenarios is the fast pace of change in health care, which can increase workplace tension, frustration, and loss of engagement.[8] Yet, few professional training programs incorporate skill development focusing on the four quadrants of the EI model, which could help to bridge this gap (**Table 1**).[9]

Educational strategies aimed at developing EI often include activities designed to promote self-awareness and social awareness, 2 core competencies in the EI framework.[10] One such strategy is the use of personality reflection tools, which are employed in many professional settings to catalyze discussions about interpersonal differences. Instruments such as the Myers–Briggs Type Indicator, DISC, and True Colors (TCs) have been used in both corporate and academic settings to prompt reflection on communication styles and behavioral tendencies.[11-13] In addition, there is the tool known as the Thomas Kilmann Instrument,[14] which measures baseline conflict management styles. Studies have shown a significant positive correlation between residents' collaborating scores and the faculty Accrediation Council for Graduate Medical Education competency evaluations of medical knowledge, communication skills, problem-based learning, system-based practice, and professionalism.[15] Interprofessional conflict is highly prevalent in clinical settings; a survey of physicians from 24 countries found that 71% reported conflicts occur frequently, and more than 80% described these conflicts as harmful.[16] While such conflicts can negatively impact team dynamics, they also create opportunities to improve patient care by prompting reflection on treatment and management approaches. In this context, the TC assessment provides a practical tool to increase self-awareness and help individuals recognize differences in communication and decision-making that can enhance teamwork, collaboration, and ultimately patient outcomes.

While personality assessments of this kind are not supported by strong psychometric validation,[17] they may still hold educational value when used to support introspection and dialog. The TC system categorizes individuals into four temperament groups—Gold, Green, Blue, and Orange—each representing a primary interpersonal orientation (**Figure 1**). In this model, Gold individuals, structured and dependable; Green individuals, analytical and independent; Blue individuals, empathetic and communicative; and Orange individuals, spontaneous and adaptable.

In our department, we sought to use the TC framework not as a diagnostic tool, but as a conversational springboard for promoting social awareness. This project was integrated into an EI-based leadership development curriculum for residents and designed to support broader interprofessional engagement. While the results are not intended to be generalizable, we hypothesized that they would provide insight into personality diversity within an academic cancer center and serve as a starting point for team-based educational discussions.

Materials and Methods

Research Design

This descriptive analysis was an institutional review board (IRB)-exempt educational quality improvement initiative conducted in the Department of Radiation Oncology at our NCI-Designated Comprehensive Cancer Center. The primary aim was to map interpersonal style diversity within the department using the TC personality framework as a foundation for leadership and communication-based education.

Survey Development and Distribution

The TC personality assessment was used to classify participants into one of four primary personality types based on value-driven behavioral preferences. These were represented with the colors Gold, Green, Blue, and Orange (**Figure 1**). This test was developed over 40 years ago to reliably predict individual profiles. The TC Assessment test (www.truecolorsintl.com/personality-assessment) has since been conducted on 10,000 participants to ensure data reliability, construct validity, and disparate impact as certified by the Assessment Standards Institute.

In order to maximize representation of each interprofessional group within the radiation oncology department, the first author scheduled presentations to describe the TC survey at each section's regular meetings to encourage participation. A PowerPoint presentation was developed explaining the background of each color and how this information could be used to improve working relationships. In addition, the survey was mentioned each month at department-wide faculty meetings. The survey was electronically distributed by our Patient Experience Optimization Team. Participants received their individual results and were encouraged to reflect on their interpersonal style. The study team received aggregate data by interprofessional group. No identifying or outcome-related information was collected. The survey was active for 3 months to ensure adequate time for participation.

Ethical Considerations

The project was reviewed and deemed exempt by the IRB as a nonhuman

Table 1. Core competencies forming the Emotional and Social Competence Inventory

SELF	OTHER
Self-awareness	**Social awareness**
Emotional self-awareness	Empathy, organizational awareness
Self-management	**Relationship management**
Achievement orientation, adaptability, emotional self-control, and positive outlook	Coach and mentor, inspirational leadership, influence, conflict management, and teamwork

subject quality improvement activity. Participants were informed that all responses were anonymous and would be used solely for educational purposes.

Results

Participants and Color Assignment

A total of 152 individuals completed the personality assessment. Respondents represented a broad range of roles within the department, including 14 attending physicians (n = 14/25, 56%), 14 radiation oncology residents (n = 14/14, 100%), 22 nurses (n = 22/26, 84.6%), 5 APPs (n = 5/12, 41.6%), 15 physicists (n = 15/28, 53.5%), 36 radiation therapists (n = 36/60, 60%), 12 dosimetrists (n = 12/20, 60%), 11 scheduling coordinators (n = 12/12, 91.6%), 11 research coordinators (n = 11/11, 100%), 2 research assistants (n = 2/2, 100%), 2 social workers (n = 2/2, 100%), and 8 administrative staff (n = 8/10, 80%). Primary and secondary colors were assigned if that color category received the most and second-most points on the assessment, respectively. Due to this, it is possible for a participant to have multiple primary and secondary colors in the case of point ties.

Overall Color Distribution

Among the 152 participants who completed the personality assessment, the most frequently reported primary color was Gold (n = 52), followed by Green (n = 45), Blue (n = 37), and Orange (n = 28). For secondary color rankings, Green (n = 47) and Blue (n = 46) were the most common, followed by Gold (n = 35) and Orange (n = 29) (**Table 2**).

Primary Color Distribution by Role

Role-specific analysis revealed meaningful patterns in color distribution. Gold was the dominant primary color for most roles requiring extensive patient interaction, including nurses (n = 13), scheduling coordinators (n = 5), and attending physicians (n = 6). Green was the most common primary color for physicists (n = 9), APPs (n = 2), and research assistants (n = 1). Blue was most prevalent among radiation therapists (n = 14) and residents (n = 7). Orange appeared less frequently overall but was identified as the primary color in some smaller subgroups (**Table 3**).

Secondary Color Distribution by Role

Secondary color patterns were more heterogeneous but still aligned with primary color tendencies. For example, individuals with Gold as a primary color often listed Green or Blue as secondary colors. Among residents, Green was the most common secondary color (n = 4), whereas Blue was more frequent among research coordinators and APPs. Orange was more frequently reported as a secondary than a primary color across nearly all roles (**Table 4**).

The results above represent a purely descriptive analysis of the TC distribution within a large, interprofessional, single-institutional radiation oncology department. The small sample size precludes formal statistical analysis. In addition, the TC methodology lacks psychometric validation in the peer-reviewed literature, although it has been independently validated by an independent, large volume, third-party assessment.

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Figure 1. Summary of the True Colors personality framework illustrating four primary personality types (Blue, Gold, Orange, and Green), each defined by distinct core traits, values, motivators, and stressors. The framework highlights how individual differences shape communication, decision-making, and collaboration styles.

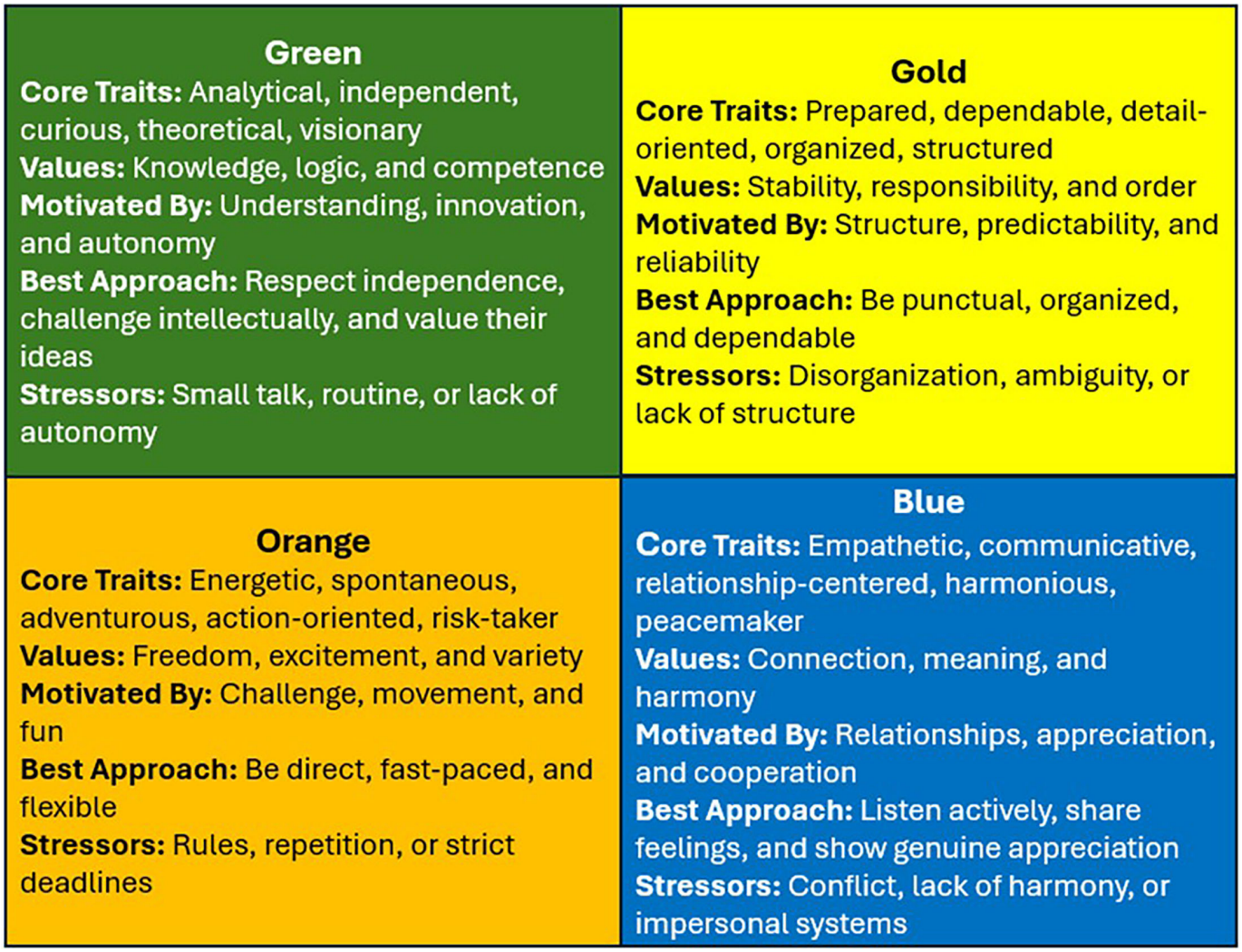

Table 2. Overall distribution of primary and secondary colors among respondents

COLOR	PRIMARY RANK N (%)	SECONDARY RANK N (%)
Gold	52 (32.1)	35 (22.3)
Green	45 (27.8)	47 (29.9)
Blue	37 (22.8)	46 (29.3)
Orange	28 (17.3)	29 (18.5)

Educational Use and Feedback

These data were presented at a departmental town hall as part of a larger educational session on EI and interpersonal communication. Each professional subgroup reviewed its own aggregate color distribution and participated in guided discussions about team dynamics, communication preferences, and leadership development. The patient experience team led the session, and although formal outcome data were not collected, qualitative feedback suggested that the exercise was well received and stimulated meaningful conversation across clinical and support teams.

One example highlighted the practical application of TC. Shortly after the TC results were distributed, there was a regularly scheduled quality improvement departmental meeting attended primarily by radiation therapists, dosimetrists, and representatives from physics. After the meeting, a conflict arose with the radiation therapists and dosimetrists, who did not feel that they had been adequately trained on the new technology that the physics group was implementing. They expressed that their concerns were minimized and devalued. When the leader heard this, he set up a subsequent meeting with the only physicist in the group who was classified as "Blue." This physicist took the time to listen to the group's concerns and explain how their point of view would be integrated into the new departmental process. The leader then created a new

Table 3. Primary color frequencies by professional role

ROLE	ORANGE (N)	GOLD (N)	BLUE (N)	GREEN (N)
Administrative staff	0	0	1	1
Advanced practice providers	0	2	0	1
Certified medical assistants	1	4	1	3
Clinical research coordinators	0	2	1	6
Dosimetrists	0	5	3	4
Nurses	1	13	3	5
Radiation oncology residents	1	3	7	3
Attending physicians	0	6	4	4
Physicists	1	3	2	9
Radiation therapists	5	7	14	10
Research assistants	1	1	0	0
Scheduling coordinators	2	5	1	3

Table 4. Secondary color frequencies by professional role

ROLE	ORANGE (N)	GOLD (N)	BLUE (N)	GREEN (N)
Administrative staff	1	1	0	0
Advanced practice providers	2	0	2	0
Certified medical assistants	2	0	0	1
Clinical research coordinators	4	2	1	2
Dosimetrists	1	2	4	4
Nurses	3	4	9	5
Radiation oncology residents	2	3	2	4
Attending physicians	0	5	3	6
Physicists	0	4	2	9
Radiation therapists	3	9	14	9
Research assistants	0	1	1	0
Scheduling coordinators	3	2	5	1

position, the physics interprofessional team coordinator, a promotion associated with a professional development role, training dosimetrists and therapists. This example aligns the physicist with the "Blue" traits, reflecting an empathetic communicative style, into a novel physics leadership position, demonstrating how awareness of personality traits can inform leadership development and professional growth.

The results were also incorporated into the radiation oncology residency leadership training curriculum with a team-based exercise whereby a medical resident and a physics resident captain both selected "teams" for an exercise involving the future structure of the anticipated proton program. Each team had a "coach" to help evaluate the questions for analysis. Each resident was asked to voluntarily disclose their TC result if comfortable, so that the captains could select balanced teams. All 14 residents did so, and then the captains were queried on how they sought to promote TC diversity on their teams and how the TC of each member would add to the team's effectiveness. This exercise reinforced the differences between TC among colleagues and deepened the understanding of how to think through team diversity. Informal feedback after this session revealed consistently high acceptance rates among the medical and physics radiation oncology residents. This exercise was designed to foster enhanced understanding of not only TC differences but also interprofessional differences since the program consists of physics residents in addition to the medical residents in radiation oncology. The success of this pilot session will be incorporated into other leadership training activities, and formal feedback will be evaluated.

Discussion

Effective interprofessional collaboration in oncology necessitates not only clinical expertise but also the nuanced interpersonal dynamics that underpin team-based care. While the TC framework lacks formal psychometric validation, its utility in this study was not to predict performance. Rather, it served as a practical and highly feasible tool that could be implemented across a large and professionally diverse department. The initiative required minimal resources, was well-received by participants from all roles, and successfully engaged individuals from clinical, technical, and administrative backgrounds. By providing a simple, accessible vocabulary for discussing personality-driven behavior patterns, the framework established a shared language that helped bridge communication gaps and catalyze constructive discussions about collaboration and team dynamics within a highly diverse interprofessional working environment.

Strengthening these teaming skills is essential to creating safer, more cohesive health care environments. Cancer care depends on highly coordinated teams.[18] In such highly complex medical environments, interpersonal conflict and burnout can directly affect patient safety by negatively influencing staff retention and work engagement.[19] Burnout has

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been shown to contribute to poor quality of care, disengagement from work, increased medical errors, hostility toward patients, difficult relationships with co-workers, and decreased commitment to patient safety.[20,21] In a national survey of over 700 radiation therapists, 76% of medical errors were discovered by either a radiation therapist or physicist, underscoring how heavily the system relies on vigilant, high-functioning teams.[22] Yet 40% of radiation therapists report that burnout and anxiety negatively affect their ability to deliver care, and 17% report experiencing workplace bullying, further heightening the risk of communication failures and team dysfunction.[22]

Frameworks such as TC can help address these challenges by providing a common language for understanding differences in communication styles, stress responses, and temperaments. This could reduce errors that stem from misunderstandings or assumptions and support psychological well-being among health care personnel.[23,24]

The Non-Technical Skills in Medical Education Special Interest Group, a global network of clinicians, educators, and researchers, defines nontechnical skills as the combination of social and cognitive abilities that collectively support safe, effective, and efficient interprofessional care within complex health care systems.[5] Their consensus emphasizes team-level competencies such as adaptability, implicit and explicit coordination, shared leadership, and conflict resolution as critical components of effective teamwork in dynamic clinical environments. By integrating these nontechnical skills with structured frameworks like TC, organizations can enhance interprofessional collaboration, mitigate burnout, and build a more resilient and reliable clinical environment.

The distribution of primary and secondary personality colors across the department revealed distinct patterns that largely aligned with professional identity. Gold was dominant in patient-facing roles, consistent with the structured, dependable, and rule-following tendencies described in the framework. Conversely, Green was more frequent in research-heavy and technical roles like physicists. These findings are intuitive but rarely discussed openly within team settings. This type of exercise brought those differences to the surface in a way that was accessible and nonjudgmental.

This study highlights the potential utility of personality mapping as a gateway to EI-based education, particularly given the increasing recognition of EI as a cornerstone of effective leadership and interprofessional collaboration in health care. The EI, especially in the domains of social awareness and relationship management, has been shown to enhance team communication and workplace culture. Foundational skills such as empathy, self-awareness, and social insight are directly linked to personal growth and leadership capacity in clinical teams.[2,25] Various models conceptualize EI as a critical competency for adaptability and professional effectiveness across medical domains.[26,27]

Curricula grounded in EI have been successfully implemented in surgical training, oncology leadership programs, and interprofessional education initiatives.[9,28] What distinguishes this initiative is its inclusion of the entire department, encompassing both clinical and non-clinical staff, in a unified reflective exercise that promotes inclusivity and broad-based engagement, which are often lacking in more narrowly focused efforts. The structure of the initiative also aligns with adult learning theory, which emphasizes autonomy, relevance, and experiential engagement as essential for motivation and retention.[29] Feedback from the departmental town hall indicated that participants found the activity both accurate and personally meaningful. Although this feedback is self-reported, the enthusiastic responses support the continued use of personality-based frameworks such as TC as accessible entry points into more advanced EI development.

From an implementation perspective, this initiative required minimal resources, suggesting that similar departments could replicate it with ease. The only logistical barriers were securing participation and scheduling town hall-style follow-up sessions. Importantly, faculty leadership support was critical to the normalization of the activity. In future iterations, expanding the initiative to include structured follow-up modules or conflict-resolution simulations may offer even greater utility.

A limitation of the TC instrument is that it has not undergone rigorous external validation. Indeed, the TC methodology lacks psychometric validation in the peer-reviewed literature, although it has been independently validated by an independent large-volume third-party assessment. The results above thus represent a purely descriptive analysis of the TC distribution within a large interprofessional single institutional radiation oncology department. The small sample size also precludes formal statistical analysis. In light of this, we deliberately refrained from positioning the framework as a diagnostic or predictive tool. Rather, it was employed as a reflective exercise to facilitate team-based dialog. Additionally, behavior change, communication quality, or team dynamics measurements were not included. As such, the findings should be interpreted as descriptive and exploratory, serving as a foundation for future hypothesis-driven work.

Future research might pair this type of initiative with validated tools like the Jefferson Scale of Empathy[30] or the Emotional and Social Competency Inventory[31] to explore whether personality reflection leads to measurable change. Alternatively, longitudinal data could assess whether individuals alter their communication approaches based on team composition awareness. Lastly, qualitative interviews could help explore how individuals

internalize and respond to personality-based feedback in clinical practice.

Conclusion

This department-wide initiative used the TC framework as a reflective tool to promote EI and team awareness. Personality distributions aligned with professional roles and helped initiate discussions on communication and collaboration. The tool was incorporated into our Radiation Oncology Leadership Training course with a pilot team-based module with high informal positive feedback, suggesting a role for further training with formal evaluation. A new physics leadership role was created in direct response to the exercise, creating a novel leadership position for a faculty member whose assessment revealed his Blue TC and aligned to the departmental need for an empathetic communicator. While not a validated assessment, the tool supported educational goals and offered a practical entry point for EI training in academic oncology.

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Treatment of Stage IIB Seminoma in a Patient With Down Syndrome and Eisenmenger Syndrome: A Case Report

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Abstract

Background Management of testicular germ cell tumors in patients with complex comorbidities remains challenging. We present a case of stage IIB seminoma in a patient with Down syndrome (DS) and Eisenmenger syndrome (ES).

Case Presentation A 37-year-old man with DS and ES underwent radical orchiectomy for a testicular mass, confirming seminoma (pT2N2M0R0S0). Following disease progression during surveillance, external beam radiation therapy (36 Gy in 18 fractions) was administered using a dog-leg field technique, as both chemotherapy and surgery were contraindicated. Treatment was well-tolerated with only mild nausea. Follow-up imaging showed near-complete response at 4 months, with stable disease at 12-month follow-up.

Conclusion This case demonstrates radiation therapy as an effective, well-tolerated treatment for stage IIB seminoma. Despite theoretical concerns regarding radiosensitivity in DS and the hemodynamic risks of thoracic irradiation in ES, standard para-aortic/iliac radiation was delivered safely, achieving disease control without unexpected toxicity.

Keywords: seminoma, Down syndrome, Eisenmenger syndrome, radiation therapy, testicular cancer

Introduction

Testicular germ cell tumors (TGCTs) represent 1% to 2% of all cancers in men and are the most common solid tumors found in male adolescents and young adults.[1] Most testicular tumors (95%) arise from germ cells and can be divided into seminomas and non-seminomas, each with distinct biological behaviors and treatment responses.[2,3]

Treatment approaches for TGCTs vary according to histological subtype and disease stage. For stage IIB seminomas (characterized by metastasis with a lymph node mass between 2 and 5 cm in greatest dimension; or >5 nodes, positive, and none larger than 5 cm; or evidence of extranodal extension of the tumor), several treatment options exist, including radiation therapy (RT), chemotherapy (CT), and retroperitoneal lymph node dissection (RPLND).[4-6] Historically, RT has maintained a crucial role in the treatment of these tumors, with stage IIA seminoma typically treated with 30 Gy to the para-aortic and ipsilateral iliac lymph nodes and stage IIB seminoma treated with an escalated dose of 36 Gy.[7]

Multiagent CT regimens, particularly bleomycin, etoposide, and cisplatin or etoposide and cisplatin, have become the preferred first-line approach to treating most stage II seminomas due to their efficacy and, potentially, lower long-term toxicity profiles. However, there are limited data on the outcomes of these regimens in patients with significant comorbidities or genetic syndromes,

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representing a substantial knowledge gap in the literature.[8]

Down syndrome (DS), characterized by trisomy 21, presents a unique cancer predisposition profile, where the incidence of testicular cancer is 5-fold that of the general population.[9-12] In addition, evidence has suggested a radiosensitive cellular phenotype in DS, linked to superoxide dismutase (SOD1) overexpression and defective DNA synthesis checkpoints after γ-irradiation.[13,14] However, clinical studies have not demonstrated excess RT-related toxicity in this population.[15]

Eisenmenger syndrome (ES) is particularly prevalent in individuals with DS.[16] The condition limits cardiopulmonary reserve in these patients, significantly constraining oncological management options.[17-19] In this context, field selection is critical: para-aortic and iliac RT fields largely spare the heart and lungs, thereby minimizing hemodynamic stress, whereas thoracic fields may exacerbate pulmonary hypertension and right heart strain. For such patients, RT may offer advantages by avoiding systemic toxicities, though the patient's cardiac and pulmonary function must be carefully factored into treatment planning.[20,21]

The aim of this case report is to highlight the management of stage IIB seminoma in a patient with DS and ES, while demonstrating the value of RT as a treatment modality in this unique clinical scenario.

Case Presentation

A 37-year-old patient with a medical history of DS and ES presented for treatment with an enlargement of the left testicle, noticed by his parents. The patient had undergone previous surgery for a sacrococcygeal fistula and had no history of smoking or alcohol consumption. There were no relevant chronic medications, no known drug allergies, and no family history of oncological diseases.

The patient was comfortable at rest, without any pain, fever, weight loss, or other symptoms. Examination revealed a mass on his left testicle without inguinal or other palpable adenomegalies. A scrotal ultrasonography revealed a well-defined left testicular solid tumor, with heterogeneous echogenicity. Following admission, routine blood work showed a mildly elevated white cell count at 12.4×10^9/L and a β-human chorionic gonadotrophin slightly elevated at 5.98 mIU/mL. All other blood markers, including tumor marker levels of α-fetoprotein and lactic dehydrogenase, were within normal range. A thoraco-abdominal-pelvic tomography (CT-TAP), performed in the same month, revealed a retroperitoneal left para-aortic lymphadenopathy, located below the renal vein, measuring 20 mm, suggestive of metastatic spread. A large heterogeneous expansive lesion was identified (**Figure 1**).

The patient, through family representatives, declined both sperm cryopreservation and testicular prosthesis placement. A left inguinal orchiectomy was performed. The postoperative course was complicated by scrotal hematoma formation. The histopathological exam confirmed a left testicular seminoma, categorizing the tumor into pT2N2M0R0S0 with invasion of rete testis and >4 cm.[22] Given the patient's complex clinical history with significant comorbidities, the Urology Multidisciplinary Tumor Board recommended active surveillance rather than adjuvant therapy.

During the surveillance period, a follow-up CT-TAP at 4 months revealed, of oncological significance, a retroperitoneal lateroaortic lymphadenopathy, with the largest node measuring 23 × 22 mm, suspicious for nodal metastasis.

Given these findings, particularly the enlarging retroperitoneal lymphadenopathy consistent with stage IIB seminoma, the patient was again presented to the Urology Tumor Board, which recommended external beam RT with curative intent, specifically dog-leg field RT. Due to his comorbidities, the patient was deemed unsuitable for CT.

The patient subsequently underwent RT treatment with a 3 DCRT dog-leg technique, receiving a total dose of 20 Gy to the lumboaortic and iliac regions followed by an additional dose (boost) of 16 Gy to the left lateroaortic mass, 2 Gy per fraction, with a total dose of 36 Gy in 18 fractions, once daily (**Figure 2**). Thoracic organs were outside the field; reported metrics were therefore negligible (mean ≈ 0 Gy, V5 ≈ 0%), eliminating cardiopulmonary exposure. Measures were taken to avoid epileptic spasms, including continuous pulse oximetry, avoidance of hypoxia/hypercarbia, and cardiology oversight. No anesthesia or sedation was required.

The patient tolerated treatment well, experiencing only mild nausea, with no other documented symptoms. A reassessment CT-TAP scan after 3 months revealed a reduction in left lateral aortic adenopathy to 13 × 10 mm, with the disappearance of the remaining metastatic lymph nodes.

Since undergoing RT, the patient has remained in good health, asymptomatic, and free of treatment-related toxicities. Follow-up imaging at 1 year revealed a complete response (CR) regarding the left lateroaortic adenopathy according to RECIST criteria (**Figure 3**).[23] The patient remains stable at 12-month follow-up.

Discussion

This case report demonstrates the successful management of stage IIB seminoma in a patient with DS and ES using adjuvant RT. The CR achieved with minimal toxicity highlights RT as an effective option in this complex clinical scenario.

The most relevant finding of our case is that standard RT protocols can safely and effectively treat stage IIB seminoma in patients with DS and ES. The patient's excellent response—significant nodal reduction at 1 month and CR per

Figure 1. Thoraco-abdominal-pelvic CT. axial (left, A) and coronal (right, B) images demonstrate a retroperitoneal left para-aortic lymphadenopathy, located below the renal vein, measuring 20 mm.

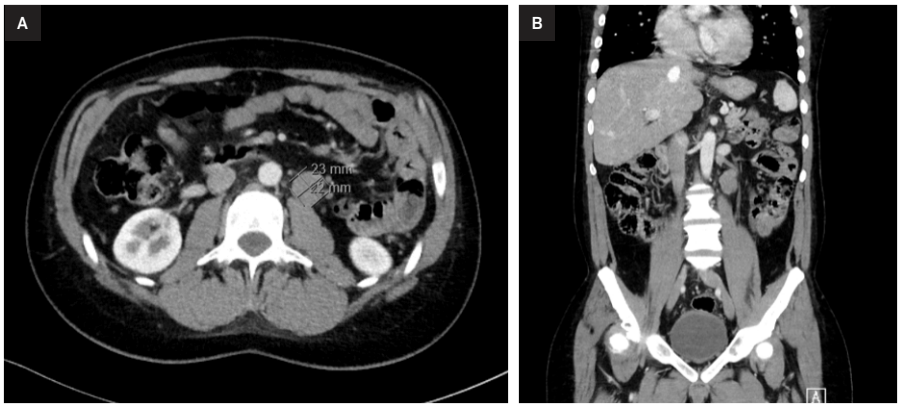


Figure 2. External beam radiation therapy treatment planning. Axial (A) and coronal (B) CT images with overlaid dose distribution and target volume (green outline).

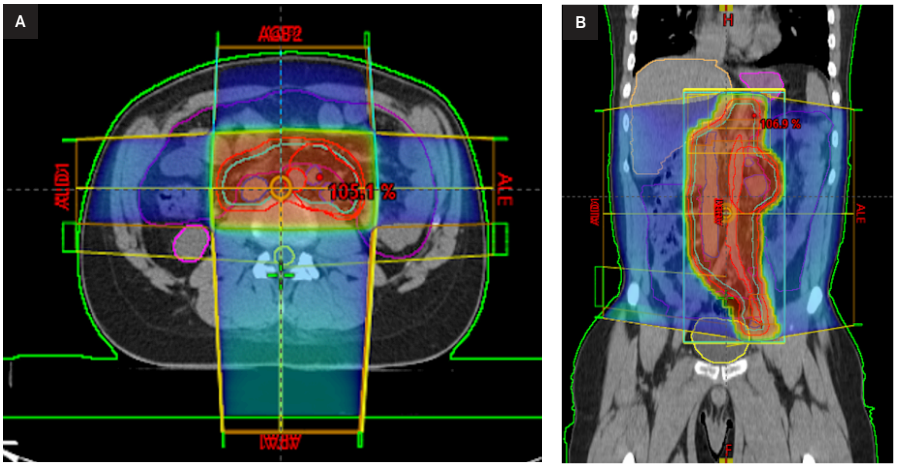
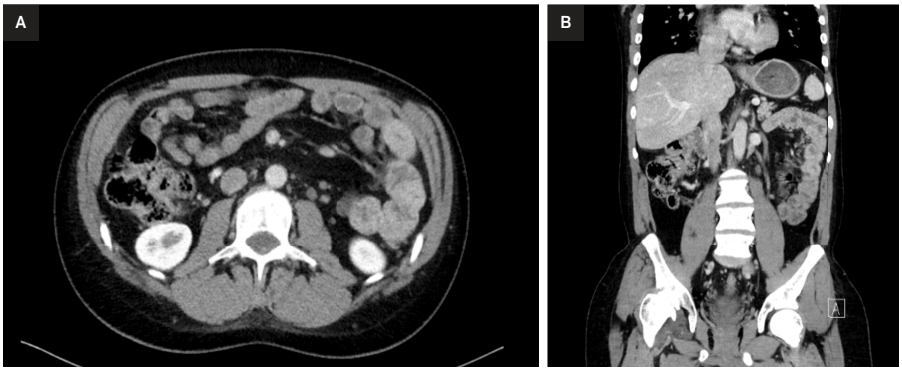


Figure 3. Reassessment thoraco-abdominal CT with 3-dimensional reconstruction at 3 m. Axial (A) and coronal (B) views demonstrate reduction in left lateral aortic adenopathy (now measuring 13 × 10 mm) with disappearance of previously identified metastatic lymph nodes.



RECIST criteria at subsequent follow-up —reinforces the high radiosensitivity of seminoma even in patients with complex comorbidities. This outcome is consistent with established data showing 5-year relapse-free survival rates of 90% for stage IIB seminoma treated with RT.[24]

The favorable toxicity profile observed in this case is particularly noteworthy given long-standing theoretical concerns regarding altered tissue radiosensitivity in individuals with DS.[25] Historically, increased radiosensitivity in DS has been postulated based on early in vitro findings showing reduced survival of DS fibroblasts after irradiation, potentially linked to overexpression of Cu/Zn-SOD1, encoded on chromosome 21.[13] Additional studies have reported abnormal DNA synthesis checkpoints following γ-irradiation in DS cell lines, suggesting an impaired DNA damage response.[14] Although these biological observations imply a predisposition to heightened radiation sensitivity, clinical data remain inconsistent, and no definitive contraindication to standard RT regimens has been established. In the present case, the absence of significant acute or subacute toxicities following a total dose of 36 Gy further supports that contemporary RT techniques and conventional fractionation can be administered safely in DS patients with appropriate monitoring.

Our approach aligns with historical practice in which RT was the primary treatment for stage IIA/B seminoma, with recommended doses of 36 Gy for stage IIB.[7] However, it diverges from contemporary trends that favor multiagent CT regimens as first-line treatment.[26,27] This decision was justified by the patient's unique clinical context, where bleomycin-containing regimens posed substantial pulmonary toxicity risks.[19] The anatomic distribution of stage IIB seminoma allowed the use of dog-leg fields confined to the para-aortic and ipsilateral iliac regions. This strategy completely avoided lung and heart irradiation, eliminating additional cardiopulmonary burden—a critical factor in patients with ES.

While recent literature has explored de-escalation approaches, such as carboplatin combined with involved-node RT as in the SAKK 01/10 trial, these approaches lack sufficient evidence for routine clinical use, particularly in patients with complex comorbidities.[28] Similarly, although RPLND has emerged as an alternative

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with 2-year recurrence rates of 18%, the substantial perioperative risks associated with ES made this approach prohibitively dangerous for our patient.[5,29]

Our case addresses a critical knowledge gap regarding testicular cancer management in patients with DS and cardiovascular complications. Patients with DS paradoxically show 5-fold higher rates of TGCTs despite lower solid malignancy rates, suggesting specific genetic, developmental, or hormonal factors possibly linked to higher cryptorchidism prevalence.[30,31] The successful outcome in this case demonstrates that RT can serve as an effective therapeutic modality, providing an important treatment option for similar patients where the standard approaches might pose unacceptable risks.

The initial decision to pursue active surveillance followed by prompt RT upon disease progression exemplifies the value of tailored approaches based on individual risk factors and disease characteristics. The integration of urological, radiation oncology, medical oncology, and cardiology expertise was essential in formulating an optimal treatment plan, highlighting the importance of multidisciplinary tumor boards in managing complex oncological cases. Despite theoretical concerns about RT in patients with DS, our case suggests that standard dose-fractionation schedules can be safely administered with appropriate monitoring and supportive care.

This report strengthens the limited clinical evidence suggesting that theoretical radiosensitivity in DS does not preclude the safe use of standard RT regimens. When delivered with precise planning that avoids thoracic exposure, RT may represent the safest and most effective curative modality in patients with seminoma and ES.

As a single case, this report cannot establish definitive recommendations, and longer follow-up is required to assess late effects and secondary malignancies. Nevertheless, it highlights a scenario where RT provided excellent disease control with negligible toxicity in a patient population that often falls outside the evidence base of clinical trials. Further research is warranted to elucidate characterization of testicular cancer in DS, evaluate different treatment modalities, and develop tailored surveillance protocols for this high-risk population.

In conclusion, RT can represent a safe and effective treatment modality for stage IIB seminoma in patients with DS and significant cardiovascular comorbidities such as ES. This approach offered excellent disease control while avoiding the potential complications associated with systemic therapy or surgical management in this medically complex patient.

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