ACR–ARS PRACTICE PARAMETER FOR THE PERFORMANCE OF TOTAL BODY IRRADIATION

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PREAMBLE

This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care[1]. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the practitioner considering all the circumstances presented. Thus, an approach that differs from the guidance in this document, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in this document when, in the reasonable judgment of the practitioner, such course of action is indicated by variables such as the condition of the patient, limitations of available resources, or advances in knowledge or technology after publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document may consider documenting in the patient record information sufficient to explain the approach taken.

The practice of medicine involves the science, and the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to the guidance in this document will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The purpose of this document is to assist practitioners in achieving this objective.

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1 *Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing, 831 N.W.2d 826 (Iowa 2013) Iowa Supreme Court refuses to find that the "ACR Technical Standard for Management of the Use of Radiation in Fluoroscopic Procedures (Revised 2008)" sets a national standard for who may perform fluoroscopic procedures in light of the standard's stated purpose that ACR standards are educational tools and not intended to establish a legal standard of care. See also, Stanley v. McCarver, 63 P.3d 1076 (Ariz. App. 2003) where in a concurring opinion the Court stated that "published standards or guidelines of specialty medical organizations are useful in determining the duty owed or the standard of care applicable in a given situation" even though ACR standards themselves do not establish the standard of care.*

I. INTRODUCTION

This practice parameter was revised collaboratively by the American College of Radiology (ACR) and the American Radium Society (ARS).

Total body irradiation (TBI) is a radiotherapy technique that may be used as a component of preparative regimens for hematopoietic stem cell transplant (HSCT) [1]. TBI, in conjunction with systemic agents, has proven useful for eradicating residual malignant or genetically disordered cells, ablating hematopoietic stem cells, and immunosuppression to reduce the risk of graft rejection.

According to data summarized by the Center for International Blood and Marrow Transplant Research, in 2019 the diseases most commonly treated with HSCT were (in decreasing order of disease frequency) multiple myeloma, non- Hodgkin lymphoma, acute myelogenous leukemia, myelodysplastic syndrome/myeloproliferative disease, acute lymphoid leukemia, Hodgkin disease, and additional malignant and nonmalignant diseases [2]. TBI has been used for many of these diseases but is not routine for all HSCT (eg, TBI is not commonly used for multiple myeloma transplants), and ongoing studies are evaluating the effectiveness of TBI-containing conditioning regimens as compared with chemotherapy alone for individual diseases [3-9]. HSCT is considered autologous if native stem cells are reinfused and allogeneic if the hematopoietic graft is derived from someone other than the recipient. Autologous is less toxic but also lacks graft versus tumor effect. Allogeneic grafts can be from related or unrelated individuals, but donor matching is preferred; the characteristics of matching impacts both the propensity for GVH and the strength of the graft versus tumor effect. The graft may be in the form of bone marrow, peripheral stem cells, or umbilical cord blood [10].

Unique features of TBI that make it a valuable component of transplant preparative regimens include:

1. Assists in eradication of malignant cells.
2. Highly effective immunosuppressive agent, even at low doses, to prevent graft rejection.
3. No sparing of "sanctuary" sites such as testes and the central nervous
4. Dose homogeneity to the whole body regardless of blood supply (in contrast to chemotherapy).
5. Less chance of cross-resistance with other antineoplastic agents (chemotherapy).
6. No problems with excretion or detoxification,
7. Ability to tailor the dose distribution by shielding specific organs or by "boosting"

A wide variety of TBI dose and fractionation schedules have been studied. The optimal regimen depends on a range of clinical variables, including patient age, disease, and type of HSCT. With competing goals of disease eradication and avoidance of toxicity, the most commonly accepted total dose of TBI for myeloablative HSCT is 12 to 15 Gy delivered in 6 to 12 fractions over 3 to 5 days [11-15]. Numerous investigators have shown that efficacy is improved and a variety of important late toxicities are significantly decreased when TBI is fractionated in 2 to 3 treatments per day [16,17]. In the case of fractionated TBI (as opposed to the historical use of single session TBI with doses greater than 2-6 Gy), along with lung shielding that is sometimes used, dose rate may have relatively less effect on toxicities [18-23]. However, relatively low dose rates may still be important for reducing the risk of interstitial pneumonitis and some other acute or late normal tissue effects such as nausea [25,26]. Indeed, many protocols require a dose rate of less than 0.2 Gy per minute, some as low as 0.1 Gy per minute. Of note, there are also both prospective and retrospective data that report an apparent dose rate effect [26-30] as well as studies that report no statistically significant dose rate effect. Dose rate therefore remains an active area of investigation in both the conventional setting (where instantaneous dose rate can be varied) and in more modern rotational techniques, in which average dose rate is the relevant variable [12,24,31-33].

Low-dose TBI, often in conjunction with chemotherapy, has recently emerged as an effective form of conditioning in reduced intensity HSCT for patients who may not be able to tolerate myeloablation because of poor performance status or age (ie, age >55 years old), undue risk due to comorbidities, or cumulative cytotoxic chemotherapy exposures. Low-dose TBI is used in reduced intensity and nonmyeloblative HSCT to reduce the likelihood of graft rejection by its immunosuppressive effects. Notable studies have included TBI doses of 2 to 6 Gy in 1 to 4 fractions [34-38]. Low-dose TBI is also being used as part of the conditioning regimen in salvage allogeneic hematopoietic cell transplantation in patients with graft rejection [39,40].

It is essential that the complicated treatment and care of the patient receiving TBI be well coordinated among the

various subspecialties (medical oncology, radiation oncology, etc) and caregivers (physicians, nurses, physicists, psychologists, dieticians, transplant coordinators, radiation therapists, physicists, dosimetrists, etc). TBI presents a unique challenge because it results in potentially lethal myeloablation without intensive medical support and stem cell backup. Incorrectly delivered TBI may result in fatal toxicity. Anticipated short-term toxicity includes the following signs and symptoms: nausea, emesis, parotitis, xerostomia, headache, fatigue, mucositis, diarrhea, and loss of appetite [41]. Prophylactic interventions to manage these toxicities include intravenous hydration, antiemetics such as ondansetron prior to each treatment, and antimucositis agents such as palifermin [42]. Patients must be counseled regarding the risks of long-term sequelae of TBI, which vary in incidence depending on the clinical scenario, age at transplant, and TBI regimen, with unique side-effect profile inherent to the age at the time of transplant. Some intermediate and late risks may include pneumonopathy [43,44], sinusoidal obstructive syndrome (SOS) of the liver [45], kidney dysfunction [46], cataracts [24], hypothyroidism [47], infertility [48], secondary malignancies [15,49-51], growth and developmental delay in children, and neurocognitive effects [52,53]. Because of the significant risk associated with this treatment, the entire team must take great care to assure the best possible multidisciplinary care with attention to all facets of TBI.

Although the techniques of TBI vary widely from institution to institution, certain basic principles apply, such as the achievement of relative-dose homogeneity throughout the body, with the exception of intentionally shielded or boosted areas [1]. Clinical-based conventional TBI (cTBI) typically uses open beam methods with large treatment distances and vaults with Cerrobend or lead blocks for lung shielding. A beam spoiler may be used to prevent skin sparing [54]. Some centers use opposing anterior and posterior (AP-PA) fields with the patient standing upright several meters from the source and the beam pointed horizontally. AP-PA fields may also be delivered with the patient lying comfortably in decubitus position also at an extended distance from the LINAC. An alternative approach irradiates patients with lateral fields in a sitting or reclining position [55]. This latter approach is usually better tolerated by patients but can present additional dosimetric challenges that must be considered and addressed to improve dose uniformity. Very young children who require anesthesia may be treated lying on the floor with the gantry pointing downward and with the spoiler and blocks placed above the patient.

Evolving modulated TBI (mTBI) uses advanced treatment planning systems (TPS) to plan and deliver TBI with beam modulation techniques such as intensity modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT). These mTBI techniques use computed tomographic electron density data and generally involve inverse optimization planning techniques to create a homogeneous dose distribution while controlling the dosimetric volume data of the lungs. These mTBI techniques can involve rotational techniques that are either isocentric or treated at extended source-surface distances (SSD). Additionally, these techniques consider special treatment couches, surface bolusing techniques, and multi-isocentric treatment planning, imaging, and delivery methods [56,57].

In both the conventional and modulated techniques, the successful planning and delivery of TBI require close interaction and coordination among the radiation oncologists, medical physicists, dosimetrists, nurses, and radiation therapists.

II. PROCESS OF TBI

The use of TBI is a complex process involving many trained personnel who carry out highly coordinated activities.

A. Clinical Evaluation

The initial evaluation should include a detailed history, including a review of issues that may have an impact on treatment tolerance (previous radiotherapy to sensitive organs, including the spinal cord and whole brain [pediatric patients]; factors affecting pulmonary, renal, cardiac or hepatic function; presence of implanted battery operated medical devices [ie, pacemakers]; cancer predisposition syndromes [Ataxia Telangiectasia, pediatrics]; and exposure to infectious agents); past medical history, ie, prior chemotherapy or immunotherapy); physical examination; review of all pertinent diagnostic and laboratory tests, including pulmonary function studies; and communication with the referring physician and other physicians involved in the patient's care in accordance with the ACR–ASTRO Practice Parameter for Communication: Radiation

Oncology [60]. Careful review of the applicable treatment plan or clinical trial protocol for the particular disease being treated is essential since standardized institutional or cooperative group protocols are typically used for transplantation.

As with delivery of any chemotherapy or radiotherapy, policies and procedures should be in place to determine whether a female patient is pregnant before initiating any component of a transplant program, including TBI. TBI can potentially have negative effects on the developing fetus. Should a woman become pregnant or suspect that she is pregnant, she should inform her treating physician immediately for confirmation and further discussion of alternatives under the circumstances. The decision will be individual, based on a balance of risks and benefits to the patient and unborn child(ren). A range of options may include those that would prioritize preservation of the pregnancy, to elective termination.

B. Informed Consent

Prior to simulation and treatment, informed consent must be obtained, documented, and in compliance with applicable laws, regulations, or policies, in accordance with the ACR Practice Parameter on Informed Consent –Radiation Oncology [61]. This should include a detailed discussion of the benefits and potential tissue-specific acute and late toxicities of TBI, as well as the details of, rationale for, and alternatives to TBI.

C. Treatment Planning

Treatment planning for TBI requires detailed knowledge of the specific transplant program to be followed. In the conventional setting, cTBI parameters to be determined in advance of treatment include field size, collimator rotation, treatment distance, dose per fraction, dose rate, total dose, number of fractions per day, interval between fractions, beam energy, geometry to achieve dose homogeneity, bolus or beam spoilers to increase skin dose, shielding and dose compensation requirements (eg, lungs, kidneys), and boost specifications (eg, testes, chest wall, brain, craniospinal axis, etc). Patient thickness measurements should be obtained at the prescription point (which is typically at the point of maximum separation, often at the level of the umbilicus) and at other points of interest for possible dose calculations and homogeneity determinations, such as head, neck, mid- mediastinum, mid-lung, pelvis, knee, ankle, etc. Patient height is recorded to determine the appropriate source-to-patient distance to fit the patient within the beam with sufficient margin around the patient (usually greater than 5 cm). Special attention should be paid to the dramatic decrease in dose that can be seen in the field corners for many treatment units when the collimator is in the full open position.

In the modulated setting, treatment planning for mTBI requires much of the same anatomical information as for conventional, but with CT simulation data, organ-specific contouring and dose calculation algorithms based on heterogeneity corrections are now available. Patients are typically simulated in an immobilization device in the head-first-supine orientation in which their arms lie laterally on each side of the body. The CT scan length is generally considered from the head to the mid-thigh for treatment planning, and respiratory motion in the thoracic region may be taken into consideration. The lungs are delineated as the primary organ at risk. The dose prescription is generally prescribed to a planning target volume (PTV) defined as the body volume from the top of skull to the mid-thigh level, excluding the lung volumes, other OARs, and retracted from the skin [62]. However, if skin flash is desired, surface or virtual bolus may be used.

For high-dose TBI regimens, mean lung dose is often limited to 8 to 10 Gy [64,65], with recent COG trials indicating high risk of lung toxicity if the lung mean dose is not <8 Gy [25,44,66]. In the cTBI setting, lung shielding can be performed by treatment in the lateral position with the arms down and/or by use of partial (50% to 80%) transmission blocks. In some cases, partial shielding of the kidneys, thyroid, lens, liver, or parotid glands is performed. In the mTBI setting, inverse optimization is generally performed for lung sparing and OAR dose reduction. A multi-isocenter rotational or helical technique may be used with adjacent fields overlapping at least 2 cm in the longitudinal direction. Isocenters are arranged sequentially in the longitudinal direction and have the same coordinates in the lateral and anterior-posterior directions to simplify setup.

D. Simulation of Treatment

For lung or other organ blocking, simulation or other treatment planning is generally done in the treatment position (ie, if the patient is standing for TBI, the simulation should be done in the standing position if possible). As an alternative to CT simulation in the supine position, lung blocks may be designed on megavoltage radiographs generated by a linear accelerator with the patient in an upright position. If the planning session is performed in another position, positional differences in organ location should be considered, and the medical physicist should be consulted. Reference points for block placement at the time of treatment should be marked on the patient's body for reproducibility. If the patient is treated in the lateral decubitus position, reproducibility of setup may require arm positioning such that all or a portion of the lung is blocked by the arms themselves, obviating or reducing the need for additional external lung block devices.

E. Calculations

Calculations for cTBI are performed by the medical physicist or their designee to determine the beam-on time necessary to achieve the prescribed dose, dose homogeneity, and any other relevant dose points. Consideration should always be given to differences in the patient's separation in different body regions with the resulting dose heterogeneities. For example, adjustments should be considered for overweight patients who can experience severe head and neck mucositis, as well as prescription doses in excess of 20% over the cervical spinal cord when only umbilical separation is used for prescribing dose [67], or alternatively, the patient can be considered for mTBI. These considerations are especially important in patients with a history of prior radiation therapy. A medical physicist or a dosimetrist who did not perform the initial computation should independently check the calculation before the first fraction is delivered. It is recommended here that in vivo dosimetry be used to assess dose homogeneity. Every effort should be made to maintain dose inhomogeneity to within ±10%.

For mTBI, dose calculation algorithms are employed that consider heterogeneities based on the patient's CT scan. The inverse optimization techniques attempt to provide adequate PTV coverage while balancing mean lung dose and OAR constraints as well as attempting to maintain dose inhomogeneity. However, due to the shorter isocentric techniques, greater inhomogeneities than cTBI may be acceptable.

F. Treatment Aids and Imaging

Special TBI stands, treatment couches, or treatment tables are often used to aid in immobilization, placement of organ shields, and patient support and comfort. Imaging using a mega-voltage (MV) film or cassette may be done to ensure lung blocks are appropriately positioned prior to treatment. In these cases, efforts should be made to use ALARA as the guiding principle and to reduce the imaging dose and field size to the region of interest where possible [68]. For cTBI, this region would be the lungs, whereas for mTBI, the region of interest may be the next sequential isocenter or the junction region between the rotational technique used for delivery of the head to mid-thigh region abutted with an anterior-posterior beam treating the legs. These TBI imaging techniques generally involve image-guidance technologies including MV portal imaging, kilo-voltage (kV) x-ray imaging, kV cone-beam CT (CBCT) imaging, or MV CT imaging.

G. Treatment Delivery

TBI containing myeloablative transplant programs typically use fractionated or hyperfractionated regimens (twice or thrice) over several days to minimize both acute and chronic toxicities and to minimize overall treatment time. Consideration should be given to the time interval between fractions delivered on the same day (typically treatments are separated by a 4- to 6-hour interval). Prior to treatment, any shielding of normal organs should be checked clinically or with portal images. In the setting of low-dose TBI, where total doses are typically only 2 to 4 Gy, organ shielding is usually not used. Dosimetry should be checked against department protocols to verify dose delivery at the extended distances that are used for treatment. Surface dose measurements using diodes or optically stimulated luminescence detectors (OSLD) are commonly used for dose verification on the first fraction. A medical physicist should be available during all treatments in case of questions regarding dosimetric details, equipment function, patient setup, etc. Treatments are carried out by the radiation therapist per the ACR–ASTRO Practice Parameter for Radiation Oncology [58].

A physician should be in close proximity to manage any problems related to treatment. Avoidance of

medications that may cause orthostatic hypotension and the administration of IV fluids for hydration or transfusions for anemia may help to prevent syncope or near-syncopal episodes if the patient is treated in the standing position.

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

Application of this practice parameter should be in accordance with the ACR–ASTRO Practice Parameter for Radiation Oncology [58].

A. Radiation Oncologist

The radiation oncologist should be currently proficient in TBI procedures prior to embarking on any of these regimens. It is encouraged that TBI be performed in high-volume transplant centers.

The responsibilities of the radiation oncologist include:

1. Consultation and decision-making regarding the appropriate course of
2. Coordination of the patient's care with the transplantation service and other
3. Oversight and participation in the treatment planning process (immobilization techniques, simulation, block design, prescription, dosimetric and physics review, etc).
4. Review and approval of treatment verification
5. Clinical assessment of the patient's tolerance during the treatment
6. Design of boost(s), block placement for comorbidities (ie, history of previous radiation, one kidney, etc).

Continuing medical education programs should include radiation oncologists, physicists, dosimetrists, nurses, and radiation therapists. The program should be in accordance with the ACR Practice Parameter for Continuing Medical Education (CME) [69].

B. Qualified Medical Physicist

The responsibilities of the Qualified Medical Physicist include (see references [35,36] for helpful details relating to this section):

1. Establish and manage the system of dosimetric measurements, calculating and
2. Establish the system for beam-spoiling designed to adjust the dose at the beam entry
3. Initiate and maintain a quality assurance program for TBI
4. Act as a technical resource for planning of immobilization devices, dosimetry techniques, shielding, dose compensation devices, and bolus
5. Calibrate the external beam delivery system and the in vivo measurement
6. Direct supervision of dosimetry measurements and calculations for TBI
7. Verify the calculations performed by the dosimetrist

C. Dosimetrist

The responsibilities of the dosimetrist include:

1. Generation of the dose calculations for treatment
2. Dosimetry measurements

D. Radiation Therapist

The responsibilities of the radiation therapist include:

1. Setting up the patient in the treatment position, including using appropriate treatment devices
2. Verifying that the prescribed and calculated treatment distances match the used treatment distances
3. Performing and reviewing of imaging procedures to verify the setup and blocking, if any.
4. Treating the patient according to the prescription and plan provided
5. Monitoring and evaluating the patient during the treatments

E. Nurse

The responsibilities of the nurse may include:

1. Educating the patient and family about the procedures, acute/late side effects, and procedures taken

to promote safe/comfortable
2. Monitoring the patient's tolerance of the procedure to promote adequate supportive
3. Communicating any special precautions to the rest of the team regarding the care of immunosuppressed

IV. PATIENT AND PERSONEL SAFETY

A. Safety measures
Safety measures should be in accordance with the ACR–ASTRO Practice Parameter for Radiation Oncology [58].

B. Special Patient Protection Measures

1. Timing of TBI delivery must be precisely coordinated with chemotherapy regimens, procurement of stem cells, and subsequent stem cell Confirmation with the transplant team immediately before initiating TBI is important to identify any unanticipated delays or changes to the treatment plan.
2. Charting systems for prescription; delineation of treatment parameters of the setup, including any position settings of the TBI stand; and treatment delivery record, including time of delivery for multiple treatments in a
3. Physics program for calibrating the treatment machine, independent checking of dose calculations, and monitoring of dose delivery to the
4. Visual and audio contact with the patient during

V. DOCUMENTATION

Reporting should be in accordance with the ACR–ASTRO Practice Parameter for Communication: Radiation Oncology [60].

VI. EQUIPMENT SPECIFICATIONS

A treatment room large enough to accommodate extended SSD may be required for treatment of adults using conventional TBI techniques. A backup beam delivery system must be available in case of unanticipated machine failure. High-energy photon beams in the range of 4 to 18 MV are preferred for TBI. Early investigations in the use of helical tomotherapy or volumetric arc therapy for total body or selective total marrow irradiation show promise and may be used, but enrollment in clinical trial(s) evaluating this modality is highly encouraged [62,70-72]. Additional equipment may include a fluoroscopy or CT simulator, immobilization devices, equipment for the manufacture of shielding, computers for dose calculations, a beam spoiler, custom bolus, custom compensators, and dosimetry and calibration devices.

VII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education appearing under the heading *Position Statement on Quality Control & Improvement, Safety, Infection Control*, *and Patient Education* on the ACR website (https://www.acr.org/Clinical-Resources/Practice-Parameters-and-Technical-Standards).

The Medical Director of Radiation Oncology is responsible for the institution and ongoing supervision of the Continuing Quality Improvement (CQI) program as described in the ACR–ASTRO Practice Parameter for Radiation Oncology [58]. It is the responsibility of the director to identify problems, see that actions are taken, and evaluate the effectiveness of the actions.

SUMMARY

TBI is a specialized radiation technique often used prior to HSCT. Delivery of TBI requires knowledge of the clinical indications and specialized treatment setup as well as the presence of dosimetric and physics staff with training in the procedures. Safe and accurate delivery of TBI can be performed with attention to the special indications, specific morbidities, and specialized treatment delivery measurements and techniques required for this procedure.

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*As of May 2015, all practice parameters and technical standards that are collaborative with Radiation Oncology societies are approved by the ACR Council Steering Committee and the ACR Board of Chancellors and will not go through the ACR Council (ACR Resolution 54, 2015). The effective date is the first day of the month following a 60-day period that begins on the date the document was approved.

<u>Development Chronology for this Practice Parameter</u>

Adopted 2001 (Resolution 19)

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Revised 2011 (CSC/BOC)

Revised 2021 (CSC/BOC)

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