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Review Article

Proton Stopping Power in Tissue-Equivalent and Polymeric Materials: A Systematic Review

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Abstract:

Proton stopping power and water-equivalent characteristics are important factors in proton dosimetry, treatment planning, phantom development, and quality assurance. Tissue-equivalent and polymeric materials are widely used as substitutes for water in experimental and clinical applications; however, their radiological equivalence depends on material composition, proton energy, density, and the method used for characterization. This systematic review evaluates the available evidence on proton stopping power and water-equivalent characteristics of tissue-equivalent and polymeric materials used in proton dosimetry and proton therapy. Relevant studies involving experimental measurements, theoretical calculations, Monte Carlo simulations, and established stopping-power databases were reviewed, with particular attention to relative stopping power (RSP), water-equivalent ratio (WER), and water-equivalent thickness (WET). The reviewed evidence indicates that PMMA, polyethylene, and polystyrene are among the most extensively investigated polymeric materials and generally exhibit favorable water-equivalent characteristics under the conditions investigated. However, measurable differences exist among materials, proton energy ranges, and experimental or computational approaches. The findings further demonstrate that material density alone is insufficient to predict proton equivalence, as elemental composition, electron density, proton energy, and the applied physical model also influence stopping power-related quantities. Overall, appropriately characterized tissue-equivalent and polymeric materials can provide useful solid alternatives to water for selected proton dosimetry and phantom applications. Nevertheless, no material should be assumed to be universally water equivalent, and experimental or independently validated computational characterization remains necessary for applications requiring accurate proton range estimation.

Keywords: Proton stopping power, Tissue-equivalent materials, Polymeric materials, Proton dosimetry, Proton therapy, Medical physics.

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1. Introduction

The interaction of protons with matter is characterized by stopping power. This quantity is defined as the energy loss per unit path length of protons in a material caused by inelastic collisions with atomic electrons. The stopping power of protons influences the calculations of particle range and dose distribution. Therefore, stopping powers are important inputs for constructing radiation transport models in many media. Hence, stopping power underpins many applications in radiation physics, nuclear science, materials science, and medicine [1-3]. The use of proton beam radiation therapy has grown, and so has the need for stopping power data for tissue-equivalent or polymeric materials. Unlike other radiation therapy methods,

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such as photon therapy, proton therapy has a depth dose distribution with a characteristic Bragg peak. This distribution allows high doses of radiation to be deposited in the tumor region, with a considerably lower dose deposited in the surrounding healthy tissue. For proton therapy to be effective, various stopping-power-based calculations are needed to determine the dose distribution and deliver therapy. Stopping power data are crucial for all steps of proton therapy, including treatment planning, dosimetry, calibration, and the assurance of radiation therapy quality [4]. Water is the reference material for measuring proton doses because of its similarity to soft biological tissue in radiation response. Despite this, experimental and computational studies usually rely on tissue-equivalent or polymeric materials. In addition to water, many other materials that have some combination of desirable physical and radiological properties, such as polymethyl methacrylate (PMMA), polyethylene, polystyrene, A-150 tissue-equivalent plastic, Plastic Water, Solid Water, RW3, Mylar, Kapton, Lucite, and other tissue-equivalent materials, have been well studied. These materials are used in many areas of proton dosimetry, including phantom construction, treatment planning, detection system calibration, and quality assurance. These materials simulate the interaction of proton beams with biological tissue and are therefore necessary for measuring proton beam range, simulating dose, and calibrating. Therefore, reliable proton stopping power data for these materials are vital for both clinical applications and research in medical physics [5,6]. Many approaches have been used to determine proton stopping powers, including direct measurements, stopping-power calculations based on the Bethe formula, and more advanced calculations such as SRIM and PSTAR. These approaches have helped quantify proton energy loss over a wide range. However, discrepancies in the published literature remain due to variations in experimental setups, material types, and computational models. [1-4]. While there are many published studies, information on proton stopping power in polymeric and tissue-equivalent materials remains fragmented across experimental, theoretical, and computational studies. Although many studies report stopping-power data for different materials, comprehensive reviews of these studies are scarce. As such, this systematic review fills a gap in the existing literature by critically evaluating and synthesizing published studies on proton stopping power in tissue-equivalent and polymeric materials used in medical physics. Extensive attention has been given to published experimental studies, theoretical studies, Monte Carlo simulations, computational studies, application studies in dosimetry, and research gaps to guide future studies. [5,6]

2. Aim of Study

The aim of this study is to provide a critical synthesis and evaluation of articles on proton stopping power in tissue-equivalent and polymeric materials within the scope of medical physics and proton therapy. This review provides detailed information on the reported stopping power of these materials, on the measurements and theories, Monte Carlo Simulations and computational methods, and highlights their uses in dosimetry, detector calibration, development of phantoms, treatment planning, and quality assurance. It also identifies the current research voids and proposes research areas that may be of greatest interest.

3. Materials and Methods

3.1 Study Design

This systematic review evaluates publications that include data on proton stopping power in tissue-equivalent and polymeric materials utilized in medical physics and proton therapy. This review focuses on studies that examine proton stopping power, ratio, energy loss, range, and other water-equivalent parameters in tissue-equivalent and polymeric materials, including water, PMMA, polyethylene, polystyrene, A-150 tissue-equivalent plastic, Plastic Water, Solid Water, Mylar, Kapton, Lucite, and similar materials. The process was

structured to identify studies in a thorough, transparent, and reproducible manner [7].

3.2. Reporting Guideline

The preparation and reporting of this systematic review were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) Statement. This guideline outlines how to conduct and report a systematic review, including description of the review, scrutiny of studies, selection of studies, and transparency of the review process. Adherence to the PRISMA 2020 Statement facilitates improvements in a systematic review's methodology, reproducibility, and transparency [7].

3.3. Literature Search Strategy

A thorough search of the literature was conducted to find articles reporting on proton stopping power in polymeric and tissue-equivalent materials. The search strategy was broad enough to include relevant experimental, theoretical, and computational studies. No hindrance was applied to the methodology used in the original studies. The search was accomplished using different combinations of terms and vocabulary in the areas of proton stopping power, tissue-equivalent materials, polymeric materials, proton therapy, radiation physics, dosimetry, and Monte Carlo methods. Boolean operators (AND, OR) were used to refine the search and obtain more relevant publications. In addition, the reference lists of the included studies were manually examined to identify additional relevant articles that were not found in the electronic search [7,8].

3.4 Information Sources

The literature search was conducted using several major international scientific databases to ensure comprehensive coverage of the available literature. The main databases were Scopus, Web of Science, ScienceDirect, SpringerLink, and PubMed. These databases were preferred because they provide access to high-quality peer-reviewed journals in medical physics, radiation physics, nuclear science, materials science, and allied professions. Further articles were added by manually screening the reference lists of relevant articles when necessary. [7,8]

3.5 Eligibility Criteria

The eligibility criteria for this systematic review were established to ensure the inclusion of relevant, high-quality studies and the exclusion of studies that did not meet the predefined selection criteria**.**

Inclusion Criteria

1. Original peer-reviewed research articles published in scientific journals.
2. Studies investigating proton stopping power, stopping power ratio, proton energy loss, proton range, or water-equivalent characteristics in tissue-equivalent and polymeric materials used in medical physics.
3. Experimental, theoretical, computational, or Monte Carlo simulation studies.
4. Articles published in English.
5. Studies reporting sufficient methodological details and quantitative proton stopping power data.

Exclusion Criteria

1 . Edited responses.

2 .Works that focus primarily on particles other than protons.

3 .Studies on materials that are not tissue-equivalent or polymeric, or studies that have no relevance to the proton stopping power and its related dosimetric properties.

4 .Publication lacking sufficient methodological description or quantitative proton stopping power data.

5. Publications that are duplicates of other submissions.

3.6 Study Selection

After the database searches, duplicate records were removed. Studies were screened after removal of duplicates, and included the following steps: title,

abstract, and, where necessary, full-text assessment, for inclusion based on the defined eligibility criteria. Only studies that fulfilled inclusion criteria were further considered for qualitative synthesis.

3.7 Data Extraction

Data extraction for each study that was included was performed with a dedicated data extraction form for this review. Data collected included: first author's name and year of publication, country of study, examined material, proton energy range, type of study (theoretical, experimental, or simulation), computational or analytical method (e.g., SRIM, PSTAR, Monte Carlo), and main study findings regarding proton stopping power. The data collected were placed in summary tables for qualitative comparison and synthesis of the included studies.

3.8 Data Synthesis

A qualitative synthesis was performed to compare the findings of the included studies. The studies were grouped according to the tissue-equivalent and polymeric materials investigated. Comparisons were made based on the investigated material, proton energy range, computational approach, research methodology, and reported stopping power characteristics. Similarities, differences, and possible reasons for discrepancies among the published studies were critically analyzed and discussed.

4. Results

4.1 Literature Search Results

The literature search revealed some studies on proton stopping power and its dosimetric attributes in medical physics, as well as relevant tissue-equivalent and polymeric materials. After removing duplicates, title and abstract screenings were performed using our predetermined eligibility criteria. Full texts of the studies were reviewed for eligibility, and all included studies were incorporated into the qualitative synthesis. The study selection process was conducted in accordance with the eligibility criteria outlined in this review.

4.2 Characteristics of the Included Studies

The studies in this systematic review investigated proton stopping power and related dosimetric attributes in many tissue-equivalent and polymeric materials used in medical physics. The reviewed studies employed various research techniques, including theoretical calculations, direct measurements, Monte Carlo simulations, and computational methods such as SRIM and PSTAR. The materials studied included water, methyl methacrylate (PMMA) polymer, polyethylene, polystyrene, A-150 tissue-equivalent plastic, Plastic Water, Solid Water, RW3, Lucite, Mylar, Kapton, and other tissue-equivalent materials. The main characteristics of the included studies, such as publication year, materials studied, proton energy range, research approach, and main findings, are summarized in Table 1.

The reviewed studies showed a wide range of proton energies and diverse computational and analytical methods. This variety reflects the intensive research effort to obtain more accurate proton stopping power data for applications in proton therapy, radiation dosimetry, the production of radiation phantoms, and the calibration of detector systems.

Table 1. Characteristics and Main Findings of the Studies Included in the Systematic Review.

No.	Author(s), year	Investigated Materials	Proton Energy	Method/Approach	Main Finding Relevant to the Review
1	Schneider et al. (2002) [9]	Solid materials used for proton dosimetry, including water-equivalent phantom materials	177MeV	Experimental proton pencil-beam measurements	Demonstrated that replacing water with solid phantom materials can produce differences in measured dose even when proton range is correctly accounted for, mainly because of differences in inelastic nuclear interactions between water and phantom materials.
2	Zhang &Newhauser (2009) [10]	materials with different densities, elemental compositions and thicknesses	Proton energy-dependent calculations	Analytical/deterministic WET calculations based on Bragg–Kleeman and Bethe–Bloch formulations, compared with iterative numerical stopping power calculations	Developed deterministic approaches for calculating WET and evaluated their accuracy for materials with different thicknesses, densities and compositions
3	Al-Sulaiti et al. (2010) [6]	PMMA, graphite, A-150 aluminum, and copper	60 and 200 MeV	Experimental measurements + MCNPX + analytical calculations	Investigated depth-dose distributions and fluence corrections at water-equivalent depths and demonstrated the importance of material-dependent nuclear interactions in proton dosimetry.
4	de Vera et al. (2014) [11]	Water, PMMA,PS, graphite, Al, Ti, Cu and Au	50-200MeV	SEICS Monte Carlo simulation	Simulated proton Bragg curves and water equivalent properties while accounting for electronic energy loss, energy-loss straggling, multiple elastic scattering, charge exchange and nuclear fragmentation.
5	Akbari et al.(2014) [12]	PMMA, PS and Al	Different proton energies	FLUKA+SRIM	Calculated WER for PMMA, PS and Al and compared the results from FLUKA and SRIM with available experimental and simulation data
6	Grant et al. (2014) [13]	18 Phantom/tissue substitute materials	Clinical proton beam	Experimental RLSP measurements	Measured RLSP values of materials used or considered for anthropomorphic proton-therapy phantoms and evaluated their suitability for proton applications
7	Ödén et al. (2015) [14]	72 human tissues	Proton therapy relevant energies	SRIM comparison+ Bethe formula calculations	Demonstrated that assumptions concerning Bethe corrections, Bragg additivity, the water(I-value), and elemental(Ivalues) influence calculated stopping-

					power ratios used in stoichiometric calibration
8	Doolan et al.(2016) [15]	11 plastic tissue substitutes	proton beam measurement	Experimental Bragg-peak-shift measurements + RSP models	Established experimental RSP measurements for plastic tissue substitutes and compared them with several stopping-power estimation models, providing a benchmark for RSP calculations
9	Damache et al.(2016) [16]	Kapton polyimide thin film	0.9-3.4 MeV	Experimental transmission measurements + theoretical models + SRIM2008	Directly measured proton stopping power and energy loss straggling in Kapton. Stopping power uncertainty was below 2%, and experimental stopping powers showed excellent agreement with previous data and ICRU-49 values
10	Lourenço et al.(2017) [17]	Trial water-equivalent plastics and commercially available plastic materials	60 and 226 MeV	Experimental measurements + FLUKA Monte Carlo simulations	Evaluated the water-equivalence of trial and commercial plastics in clinical proton beams using the plastic-to-water conversion factor. The trial materials were experimentally characterized at 60 and 226 MeV and compared with FLUKA simulations.
11	Jassim(2017) [18]	Polyethylene, Mylar, polystyrene and Kapton	Energy dependent	Experimental databases + Mathematica + SRIM2013 + PSTAR + libdEdx	Compared experimental proton electronic stopping-power data with several databases and computational approaches and found that no single database consistently described all investigated polymers over the studied energies
12	Van Abbema et al. (2018) [19]	32 well-defined materials, mainly clinically relevant materials	Photon beam measurements	High-accuracy experimental RSP measurements + Bethe-Bloch and Geant4 comparisons	Provided high-accuracy experimental RSP reference values. Relative standard uncertainty was below 0.4% for samples with approximately 2 cm WET, providing a ground-truth benchmark for RSP
13	Safigholi& Song (2018) [20]	Various dosimetric and tissue-equivalent materials	10-500 MeV	FLUKA, MCNP, and GEANT4 Monte Carlo simulation	Calculated WER over a broad proton-energy range and provided comparative WER data using three independent Monte Carlo codes
14	Bagheri et al. (2019) [21]	PE, PP, PMM, PS, paraffin and PC	Different proton energies	MCNPX+comparison with NIST, experimental/analytical data, FLUKA, SRIM and SEICS	Calculated WER for six dosimetric materials using MCNPX and compared the results with NIST data, experimental/analytical results, and other simulation codes.
15	Cook et al. (2023) [22]	Optimized epoxy-resin tissue-equivalent materials	Proton therapy relevant conditions	Mathematical optimization + experimental characterization	Developed and characterized optimized materials that reproduced the target tissue

					properties within approximately 1-2%for mass density and RSP
16	Bento et al. (2024) [23]	PLA, PMM, PETG A, ABS, HIPS, and StoneFill	210 MeV	Experimental RSP + density/CT characterization	Evaluated six 3D-printable thermoplastics as tissue-equivalent materials. RSP was measured using a 210 MeV proton pencil beam and compared with CT-based and theoretical predictions
17	Matias et al. (2024) [24]	Organic polymers: polyethylene (PE), polystyrene (PS), poly(2-vinylpyridine) (P2VP), polyamide (PA), polyimide (PI) and PMMA	Broad proton energy range, with particular attention to energies below 2 MeV and around the stopping maximum	Real-time time-dependent density functional theory (RT-TDDFT) coupled with the Penn method; computational modeling of the spatial electron-density distribution	The study showed that assuming homogeneous electron density in organic polymers can overestimate electronic stopping power at energies below 2 MeV. It also found that application of Bragg's rule can show significant deviations from experimental data around the stopping maximum, highlighting the importance of the detailed electronic structure of polymers in stopping power calculations
18	Mbagwu (2025) [25]	Water,air, AL_2O_3, aluminum (Al), oxygen, and BaFBr	0-250MeV for the reported SPR comparisons	Theoretical calculations using Bethe–Bloch theory and semi-empirical models, with comparison of stopping-power ratios for dosimetric materials	Evaluated the stopping power ratios of different dosimetric materials for proton-therapy LET measurements. The study demonstrated substantial material-dependent differences in SPR, particularly for BaFBr and Al_2O_3 relative to water, emphasizing the importance of material-specific stopping power corrections in proton dosimetry

Abbreviations: Abbreviations: PMMA, polymethyl methacrylate; PE, polyethylene; PP, polypropylene; PS, polystyrene; WET, waterequivalent thickness; RSP, relative stopping power; SPR, stopping power ratio; WER, water-equivalent ratio; MC, Monte Carlo; MCNP, Monte Carlo N-Particle; MCNPX, Monte Carlo N-Particle eXtended; FLUKA, FLUKA Monte Carlo code; Geant4, Geometry and Tracking; SRIM, Stopping and Range of Ions in Matter; PSTAR, proton stopping power and range database; TDDFT, time-dependent density functional theory; P2VP, poly(2-vinylpyridine); PI, polyimide; LET, linear energy transfer; TE, tissueequivalent.

4.3 Proton Stopping Power in Water

Water is widely used as a reference medium in proton dosimetry and stopping-power calculations. Reference stopping power and range data for protons in water are provided in ICRU Report 49 and incorporated into the NIST PSTAR database [1,2]. These reference data provide an important basis for evaluating proton transport and energy loss in biological tissues, tissue-equivalent materials, and other materials used in proton therapy.

Accordingly, quantities related to proton stopping and water equivalence, including relative stopping power (RSP), water-equivalent thickness (WET), and water-equivalent ratio (WER), are commonly expressed relative to water. The use of water as the reference medium is particularly important when

assessing whether a tissue-equivalent or polymeric material can reproduce the proton range and energy loss characteristics required for dosimetry and phantom applications. Studies investigating stoppingpower ratios have also demonstrated that the calculated relationship between tissue and water depends on the stopping-power formalism, the mean excitation energy, and the elemental data used in the calculations [14].

4.4 Proton Stopping Power in PMMA

Polymethyl methacrylate (PMMA) is a widely used solid phantom and tissue-substitute material in proton dosimetry because of its practical properties and relatively close water-equivalent behavior. Its proton stopping and water-equivalent characteristics have been investigated using experimental measurements, analytical calculations, and Monte Carlo simulations.

Grant et al. measured the relative linear stopping power (RLSP) of 18 materials used or considered for anthropomorphic phantoms for proton radiotherapy. Their measurements included acrylic (PMMA), for which the measured RLSP was 1.21, compared with a treatment-planning system-assigned value of 1.09, corresponding to a difference of approximately 10.3%. Because the study used a 5% difference as the criterion for proton equivalence, PMMA did not meet this criterion in that particular treatment-planning calibration. These results demonstrate that the proton equivalence of phantom materials should be experimentally characterized rather than assumed based on their physical or photon-dosimetry properties [13]. De Vera et al. investigated the water-equivalent properties of materials commonly used in proton dosimetry, including liquid water, polystyrene, PMMA, graphite, aluminium, titanium, copper, and gold. Using the SEICS simulation code, they calculated proton depth-dose distributions for incident energies from 50 to 200 MeV, accounting for electron energy loss and energy-loss straggling, multiple elastic scattering, charge-exchange processes, and nuclear fragmentation. Their results showed that PMMA and polystyrene exhibited depth-dose characteristics comparable to those of liquid water, supporting their continued use as solid materials in proton dosimetry [11]. Safigholi and Song subsequently calculated water-equivalent ratios (WERs) for several materials over proton energies ranging from 10 to 500 MeV using MCNPX, GEANT4, and FLUKA. PMMA was among the materials investigated, and its mean WER was 1.13 over the energy range studied. Among the non-tissue solid materials investigated, PMMA showed the closest water-equivalent behavior. The study also demonstrated that differences between Monte Carlo codes can arise from variations in the physical models and stopping power data implemented in the codes [20]. Bagheri et al. further investigated PMMA together with polypropylene, paraffin, polyethylene, polystyrene, and polycarbonate using the MCNPX Monte Carlo code at different proton energies. The calculated WER values were compared with NIST data and with available experimental, analytical, FLUKA, SRIM, and SEICS results. This comparison provided additional evidence that PMMA is a relevant material for evaluating proton water-equivalence and stopping behavior, while also demonstrating the importance of comparing computational results with independent reference data [21]. Overall, the reviewed studies indicate that PMMA is a useful and widely investigated solid material for proton dosimetry and phantom applications, with water-equivalent behavior that is generally close to that of water but not identical. Its proton response depends on material composition, density, proton energy, and the stopping-power or range estimation method used. Therefore, PMMA should not be assumed to be universally water-equivalent; its stopping power or water-equivalent characteristics should be appropriately characterized for the specific proton energy range and application of interest [11,13,20,21].

4.5 Proton Stopping Power in Polyethylene

Polyethylene (PE) is an important polymeric material in proton dosimetry because of its relatively simple chemical composition and favorable proton-stopping and water-equivalent characteristics. It has therefore been investigated as a potential material for tissue-equivalent phantoms and other applications in proton therapy.

Grant et al. experimentally measured the relative linear stopping power (RLSP) of several materials used or considered for anthropomorphic phantoms in proton radiotherapy. For polyethylene, the measured RLSP was 1.00, compared with an RLSP value of 0.98 assigned by the treatment-planning system, corresponding to a difference of approximately 1.9%. Because the study used a 5% difference from the HU-RLSP calibration curve as a criterion for selecting materials for proton applications, polyethylene met this criterion. These findings demonstrate the relatively close protonequivalent behavior of polyethylene with respect to water under the conditions investigated [13]. Bagheri et al. investigated the water-equivalent ratio (WER) of polyethylene together with polypropylene, paraffin, polystyrene, PMMA, and polycarbonate using the MCNPX Monte Carlo code at different proton energies. The calculated WER values were compared with NIST data and with available experimental and analytical results, as well as results obtained using FLUKA, SRIM, and SEICS. This study provided additional computational data for evaluating the water-equivalent behavior of polyethylene and other polymeric dosimetric materials and demonstrated the importance of comparing Monte Carlo calculations with independent reference data [21]. The experimental and computational findings are further supported by the comparative study of Jassim, who evaluated experimental proton electronic stopping power data for polyethylene, Mylar, Kapton, and polystyrene against results from Mathematica, SRIM2013, PSTAR, and the libdEdx database. The study showed that the level of agreement between experimental data and computational databases depended on both the material and proton energy, indicating that no single database consistently reproduced the experimental data for all investigated polymers and energy ranges [18]. Overall, the available evidence indicates that polyethylene exhibits favorable proton-stopping and water-equivalent characteristics and can serve as a practical material for selected dosimetric and phantom applications. However, its suitability should be evaluated based on the specific proton energy, material composition and density, and the measurement or computational method used. Differences between experimental measurements and computational databases further emphasize that stopping power and water-equivalent parameters should be appropriately validated for the material and energy range of interest [13,18,21].

4.6 Proton Stopping Power in Polystyrene (PS)

Polystyrene (PS) is an important polymeric material investigated for proton dosimetry and tissue-equivalent phantom applications. Its suitability is related to its proton-stopping and water-equivalent characteristics, which can be evaluated by comparing its proton range and stopping-power-related quantities with those of water.

De Vera et al. investigated the depth-dose characteristics of proton beams in polystyrene and other materials commonly used in proton dosimetry using the SEICS simulation code. Proton energies ranging from 50 to 200 MeV were considered. The simulations showed that polystyrene exhibited depth-dose characteristics comparable to those of liquid water, indicating its potential suitability as a solid substitute for water in dosimetric measurements [11]

Akbari et al. evaluated the water-equivalent ratio (WER) of polystyrene, PMMA, and aluminum using the FLUKA Monte Carlo code and the SRIM program at different proton energies. The calculated results were compared with analytical, experimental, and SEICS simulation data reported in the literature. For PS, the maximum difference between the

FLUKA and SRIM calculations was approximately 0.67%, indicating close agreement between the two computational approaches. The study also showed good agreement between the calculated results and previously reported experimental data [12]

Bagheri et al. subsequently included polystyrene among six dosimetric materials: polypropylene, paraffin, polyethylene, polystyrene, PMMA, and polycarbonate, and calculated their WERs using the MCNPX Monte Carlo code at different proton energies. The calculated values were compared with NIST data and available experimental and analytical results, as well as results obtained using FLUKA, SRIM, and SEICS. For PS, the largest difference between the MCNPX and NIST results was 0.71% at 150 MeV, demonstrating good agreement between the two datasets [21].

Overall, the available evidence indicates that polystyrene exhibits favorable water-equivalent characteristics for proton dosimetry and phantom applications. Both FLUKA- and SRIM-based calculations showed close agreement for PS, while MCNPX calculations also agreed well with NIST reference data. Nevertheless, the degree of water equivalence depends on proton energy, material composition and density, and the computational or experimental method used. Therefore, the suitability of polystyrene as a water substitute should be assessed using stopping-power or water-equivalent data appropriate to the specific proton energy range and application [11,12,21].

4.7 Other Tissue-Equivalent and Polymeric Materials

In addition to water, PMMA, polyethylene, and polystyrene, several other tissue-equivalent and polymeric materials have been investigated for proton dosimetry and phantom applications. These include polypropylene, polycarbonate, paraffin, PTFE, graphite, and specially formulated tissue-equivalent plastics. Their suitability can be assessed using proton stopping-power-related quantities such as relative stopping power (RSP), water-equivalent ratio (WER), and water-equivalent thickness (WET), depending on the intended application [20-22]. Safigholi and Song evaluated WERs for compact bone, adipose tissue, PMMA, PTFE, graphite, aluminum, copper, titanium, and gold over the protonenergy range of(10–500) MeV using MCNPX, GEANT4, and FLUKA. The results showed that PMMA was the closest non-tissue solid material to water, with a mean WER of 1.13 over the investigated energy range. However, differences were observed among the Monte Carlo codes, particularly at lower proton energies and for some high-density materials, reflecting variations in the physical models and stopping-power data implemented in the codes [20]. Bagheri et al. investigated six dosimetric materials, including polypropylene, paraffin, polyethylene, polystyrene, PMMA, and polycarbonate, using the MCNPX Monte Carlo code. The calculated WER values were compared with NIST reference data and with available experimental and analytical results, as well as results obtained using FLUKA, SRIM, and SEICS. Good agreement was observed between the MCNPX and NIST results, while the WER values varied among the investigated materials. The authors also reported a positive correlation between WER and electron density, indicating that material composition and electron density are important factors in determining water-equivalent behavior [21]. The development of optimized tissue-equivalent materials has also received increasing attention. Cook et al. developed a mathematical model to formulate epoxy resin-based tissue-equivalent materials optimized for proton and photon interactions relevant to CT imaging. The study focused on vertebral bone and skeletal muscle-equivalent plastic materials. The newly developed materials were manufactured and characterized using mass-density measurements, relative stopping-power measurements, and CT imaging. The best-optimized formulations reproduced their target biological tissues within approximately 1–2% in mass density and RSP, whereas some commercial

tissue-equivalent materials showed substantially larger differences. These findings emphasize the importance of optimizing material composition rather than relying solely on commercially available phantom materials [22]. Overall, the available evidence indicates that no single polymeric or tissue-equivalent material can be considered universally equivalent to water or to all biological tissues. The degree of proton equivalence depends on elemental composition, density, electron density, proton energy, and the specific physical quantity and computational or experimental method used for characterization. Therefore, quantitative evaluation of RSP, WER, or WET remains necessary before a material is adopted for proton dosimetry, phantom construction, rangeshifter applications, or treatment verification [20-22].

4.8 Comparison of Experimental, Theoretical, and Monte Carlo Approaches

The included studies employed experimental, theoretical, and computational approaches to determine or evaluate the proton stopping power and water-equivalent characteristics of tissue-equivalent and polymeric materials. Experimental measurements provide direct reference data under defined beam and material conditions, whereas theoretical and computational approaches allow stopping power and water-equivalent behavior to be evaluated over broader energy ranges and for materials for which experimental measurements may be limited

Experimental approaches were used to determine the relative stopping power and related proton-range characteristics of selected phantom and tissue-equivalent materials. Grant et al. measured the relative linear stopping power (RLSP) of materials used or considered for anthropomorphic phantoms in proton radiotherapy, demonstrating the importance of direct measurements when assessing the suitability of phantom materials for proton applications [13]. The original study measured 18 materials and used a 5% difference relative to the treatment-planning system HU-RLSP calibration curve as the criterion for proton equivalence. Van Abbema et al. subsequently performed high-accuracy experimental RSP measurements for 32 well-defined materials with known composition and density. Their measurements yielded reference RSP values with a relative standard uncertainty below 0.4% for samples with a water-equivalent thickness of approximately 2 cm, providing experimental benchmarks for evaluating CT-based and Monte Carlo RSP calculations [19]. Experimental measurements are particularly valuable for validating treatment planning system calculations and computational models; however, their accuracy can be affected by beam energy uncertainty, detector response, material thickness and density, experimental geometry, and other measurement factors [13,19]. Theoretical calculations provide an efficient approach to estimating proton stopping power based on a material's physical and elemental characteristics. The Bethe-Bloch formalism is widely used to describe the electronic stopping power of charged particles and provides an important basis for analytical stopping-power calculations. van Abbema et al. noted that commonly used approximate RSP models based on the Bethe-Bloch formalism may omit several corrections, whereas more detailed implementations, such as those used in Geant4, can account for additional physical effects [19]. Analytical approaches are computationally efficient and can provide estimates over broad energy ranges; however, their accuracy depends on parameters such as material composition, density, mean excitation energy, and the physical corrections included in the formulation. Monte Carlo simulations are critical for evaluating proton stopping and water-equivalent characteristics. Safigholi and Song computed WERs for numerous materials over proton energies from 10-500 MeV using MCNP, FLUKA, and GEANT4. Their research demonstrated that multiple Monte Carlo codes can be used to obtain WER data, and that data from different computational methods can

differ across materials and proton energy ranges.[20]. Bagheri et al. also used MCNPX to compute WERs for polypropylene, paraffin, polyethylene, polystyrene, PMMA, and polycarbonate for various proton energies, and compared these computations with available NIST data and other analytical, experimental, FLUKA, SRIM, and SEICS data. It was found that the MCNPX and NIST data agreed well overall [21]. These studies illustrate the utility of Monte Carlo methods for evaluating proton- stopping and water-equivalent data across different materials and proton energy ranges [20,21].The NIST PSTAR database and SRIM are resources that contain stopping power and range data for comparison and for determining the validity of both experimental and computational results. Such resources are highly beneficial for determining stopping power over a broad range of energies. However, there can be significant differences in the definitions of materials, density values, physical models, and treatments of energy loss for different resources, calculations, and experiments. Therefore, the output of databases and codes should be examined in terms of the material and the energy of protons that is applicable to the intended use case. Most of the literature reviewed shows that there is no single exhaustive approach for proton stopping power. Measurements performed in a laboratory serve as a benchmark; calculations and modeling become more convenient; and extensive simulations can be performed to determine proton transport and energy loss. Therefore, the best estimate for characterizing tissue equivalents, plastics, and other materials for which polymer substitution has been used is a combination of all three approaches: comparisons and validations of independent approaches against available experimental data. This is especially important for water. This integrated approach can help diminish the uncertainty in determining the range, dosimetry, and quality assurance of the phantoms used for treatment planning.

4.9 Comparison of Reported Water-Equivalent Characteristics

The reported water-equivalent characteristics of tissue-equivalent and polymeric materials varied with proton energy, material composition, density, and the evaluation methodology. Consequently, direct comparison of numerical values between studies should be performed with caution, particularly when different definitions or estimators of water equivalent ratio (WER), relative stopping power (RSP), or water-equivalent thickness (WET) are used. For PMMA and polystyrene, Akbari et al. calculated WER values using both FLUKA and SRIM and compared the results with analytical, experimental, and SEICS data. The maximum differences between the FLUKA and SRIM calculations were 1.9% for PMMA and 0.67% for polystyrene. The authors also reported that FLUKA and SEICS showed the greatest agreement with the experimental data, with differences of ≤0.77% for PMMA and ≤1.08% for aluminum [12].

Bagheri et al. extended the comparison to six polymeric materials, including polypropylene, paraffin, polyethylene, polystyrene, PMMA, and polycarbonate, using MCNPX calculations. Their results were compared with NIST data and previously reported experimental, analytical, FLUKA, SRIM, and SEICS results. Good agreement was observed between the MCNPX and NIST data, with the largest reported difference being 0.71% for polystyrene at 150 MeV. The study also found a positive correlation between WER and electron density and reported that polyethylene exhibited the most analogous depth-dose characteristics to those of liquid water among the investigated materials [21].

The results reported by de Vera et al. further demonstrated that PMMA and polystyrene can exhibit depth-dose characteristics comparable to those of liquid water. Using the SEICS simulation code, the authors investigated proton energies ranging from 50 to 200 MeV and included electronic stopping power and energy-loss straggling, multiple

elastic scattering, electronic charge-exchange processes, and nuclear fragmentation in their simulations. Their results showed that solid plastics such as polystyrene and PMMA presented depth-dose characteristics comparable to those of liquid water under the investigated conditions [11]

Taken together, these findings indicate that PMMA, polystyrene, and polyethylene are among the extensively investigated polymeric materials for proton dosimetry and phantom applications, but their water-equivalent behavior should not be considered an intrinsic constant independent of experimental or computational conditions. Proton energy, material composition, density, electron density, and the physical model or computational code used can all affect the reported WER or RSP. The relatively small differences reported between independent computational approaches for PMMA and polystyrene support the reproducibility of their water-equivalent estimates under the investigated conditions; however, their suitability as practical solid substitutes for water should still be assessed for the specific energy range and application [11,13,20,21]

4.10 Research Gaps Identified from the Included Studies

Despite the growing number of studies investigating the proton-stopping power and water-equivalent characteristics of tissue-equivalent and polymeric materials, several gaps remain in the literature. **First**, substantial heterogeneity exists among the investigated materials, proton energy ranges, material compositions, and experimental or computational methodologies. This heterogeneity makes direct comparison of reported stopping power, relative stopping power, and water-equivalent data between studies difficult. Studies evaluating PMMA and polystyrene, for example, have employed different combinations of experimental measurements, analytical calculations, SEICS, FLUKA, and SRIM, with generally close agreement but measurable differences between the approaches [11,12,18]. **Second**, the available evidence is not uniformly distributed across all tissue-equivalent and polymeric materials. PMMA, polyethylene, and polystyrene are among the most extensively investigated polymeric materials, whereas fewer studies have systematically characterized other polymeric and tissue-equivalent materials across broad protonenergy ranges. Bagheri et al., for example, evaluated polypropylene, paraffin, polyethylene, polystyrene, PMMA, and polycarbonate using MCNPX and compared the calculated WER values with NIST data and previously reported experimental and computational results. This study illustrates both the diversity of candidate materials and the need for standardized comparative characterization [21].

Third, differences in material composition and physical properties remain important sources of variation in water-equivalent calculations. Water-equivalent behavior cannot be reliably inferred from material density alone because WET and related quantities depend on material composition, density, thickness, proton energy, and the stopping-power data or approximation used. Zhang and Newhauser demonstrated that the accuracy of analytical WET approximations depends on target thickness and material composition, with different formulations being required for radiologically thin and thick targets. Their results also showed that simple approximations may be adequate for thin or low-Z targets, whereas more appropriate thick-target formulations are required for radiologically thick, high-Z materials [10].

Fourth, greater consistency between experimental measurements and computational databases or simulation codes remains desirable. Studies comparing FLUKA, SRIM, SEICS, and MCNPX have often shown reasonable agreement, but measurable differences remain depending on the material and proton energy range. For example, Akbari et al. reported maximum differences of approximately 1.9% between FLUKA and SRIM for PMMA and 0.67% for polystyrene. Such differences

demonstrate the importance of validating calculated stopping power and water-equivalent parameters against independent reference data before their application to dosimetry or phantom characterization [12]. **Finally**, few studies have combined rigorous experimental characterization with independent computational verification across a wide clinical proton energy range for the same materials. Integrated studies enable the detection of discrepancies among analytical approaches, including Monte Carlo simulations, stopping-power data, and measurements. These discrepancies may help improve proton range prediction, dose estimation, proton therapy planning, phantom development, and quality assurance in proton therapy. It is apparent that the existing gaps call for the development of stopping-power and water-equivalent data for tissue-equivalent and polymeric materials within the proton energy ranges of interest, to be provided on a standardized, comparable basis. Further, to enhance proton range prediction and improve dose estimation, it would be desirable to perform coordinated experimental measurements, validate theoretical and Monte Carlo studies, and report the measurements in a standard manner. The reporting should include the material, its composition, density, proton energy range, method of measurement or calculation, and inclusion of associated uncertainties.

5- Discussion

This systematic review illustrates the dependence of the proton stopping power and water-equivalent properties of tissue-equivalent and polymeric materials on various physical and methodological factors. In the included studies, water was used as the reference material by default. PMMA, polyethylene, polystyrene, and other tissue-equivalent materials exhibited varying degrees of consistency with water under different proton-energy and measurement conditions. ICRU reference data and stopping power databases provide an important framework for proton stopping power and range calculations, demonstrating the value and reliability of these data for estimating proton penetration and energy deposition [1,3]. One of the first conclusions from this study is that proton equivalence cannot be inferred solely from material density. The proton stopping power depends on the material's composition, electron density, mean excitation energy, and proton energy. It can therefore happen that two materials of the same physical density exhibit different proton stopping powers. This is very significant when considering the development of tissue substitutes for proton therapy, since the proton range is uncertain due to uncertainty in relative stopping power [10,15]. Also, the reviewed data illustrates the complementary role of experimental and computational methods. Evidence provided by experimental measurements offers direct proton beam-material interaction characterizations, and therefore offers an important benchmark for verifying and validating theoretical and Monte Carlo calculations. For instance, comparative studies of tissue substitute materials have shown that measured RSP values can serve as references for evaluating stopping-power models. One comparison of RSP estimation methods found mean errors of about -0.1%, +0.7%, and -0.8% for the Bichsel, Janni, and ICRU methods, respectively, compared to measurements. For the Schneider method, larger deviations were found [15]. These results suggest that the choice of RSP method and specific parameters can yield different RSP values . The use of Monte Carlo methods is justified because they enable modeling of proton transport, energy, and other interactions in a controlled environment. The studies reviewed here have implemented different Monte Carlo codes, including MCNP/MCNPX, FLUKA, and Geant4. Comparative studies of different computational methods provide evidence on the materials and energy ranges for which adequate experimental data may not be available [20,21,26]. However, differences among computational methods may arise from the materials, proton energies, physical

models, and stopping power data incorporated into each code. Therefore, agreement among computational methods cannot circumvent the need for measurement validation. Another observation is the continued use of PMMA, polyethylene, and polystyrene as solid materials in proton dosimetry and phantom applications. There are many advantages, such as availability, mechanical stability, and well-known radiological properties. However, these materials should be evaluated on a case-by-case basis for the specific proton energy range and application. There is a certain level of risk in assuming a material is water-equivalent. This is more applicable to range shifters and phantoms, where the total water-equivalent thickness of the phantom is important because it affects the proton range. [13,20,21]

The development of optimized tissue-equivalent materials is another step toward improved proton dosimetry. Cook et al. showed that, through appropriate material formulations, it is possible to mimic proton-stopping phenomena in addition to making the material CT-equivalent. Their optimized materials achieved target tissue mass density and RSP within 1-2%, whereas some commercially available materials resulted in larger uncertainties in the proton range [22]. These results show that it may be more beneficial to consider multiple radiological characteristics of a material and optimize based on them, rather than optimizing a material based on a single property .The results presented also help with proton treatment planning. A large part of proton range calculations relies on converting patient or phantom materials into a stopping-power quantity. A poorly characterized material substitute can contribute to the unpredictability of the proton range. This further emphasizes the significance of characterizing tissue equivalences for the verification of treatment plans, the design of range shifters, the calibration of detectors, and the end-to-end quality assurance of the entire process [6,20] . The results also help in proton treatment planning. A large part of proton range calculations relies on converting patient or phantom materials into a stopping-power quantity. A poorly characterized material substitute can contribute to the unpredictability of the proton range. This further emphasizes the significance of characterization of tissue equivalences for the verification of treatment plans, the design of range shifters, and the end-to-end quality assurance of the entire process[6,20].

Six 3D-printable thermoplastics, including polylactic acid (PLA), acrylonitrile butadiene styrene (ABS), polylactic acid (PETG), polymethylmethacrylate (PMMA), high impact polystyrene (HIPS), and StoneFil, were analyzed. Experimental measurements of relative stopping power were carried out using a 210 MeV proton pencil beam. The study identifies several 3D-printable materials for use in tissue-equivalent components of multimodal radiotherapy end-to-end quality assurance systems. It also demonstrates the importance of experimental characterization rather than relying on the nominated material composition [23]. The available data suggest that an integrated approach is more appropriate, where experimental measurements, theoretical values, Monte Carlo simulations, and existing reference databases are combined. ICRU reference data, NIST databases, and existing simulation software constitute essential reference frameworks, while experimental measurements remain necessary to verify the radiological behavior of the materials [1,3]. The framework outlined above further reduces the uncertainty of the approach to estimating probable ranges of protons and dosimetry, based on the novel tissue-equivalent components of 3D-printed phantoms, verification of the proton therapeutic process, and quality assurance systems.

5.1 Clinical and Dosimetric Implications

The findings of this review have important implications for proton dosimetry and clinical quality assurance. Tissue-equivalent and polymeric materials are used in solid phantoms, range shifters, detector systems, and end-to-end treatment

verification. Their suitability depends not only on their physical and radiological similarity to biological tissues but also on their proton stopping power and scattering characteristics [4,6,13].

For clinical and dosimetric applications, a material should therefore be selected according to the specific radiological quantity required, such as relative stopping power (RSP), water equivalent ratio (WER), or water-equivalent thickness (WET), and according to the proton energy range relevant to the intended application. A material that performs well as a water-equivalent material under one set of conditions may not provide the same level of equivalence under another application involving a different proton energy, material thickness, or tissue composition [10,19,20].

This distinction is particularly important because proton therapy is sensitive to uncertainties in proton range. Reliable characterization of stopping power can contribute to more accurate range estimation, improved phantom characterization and calibration, and more reliable treatment plan verification. The continued development and experimental validation of tissue-equivalent materials with well-characterized RSP values may therefore improve the consistency and reproducibility of proton therapy quality assurance procedures [13,19,26].

5.2 Strengths and Limitations of the Review

This systematic review has many strengths. It integrates experimental, theoretical, and computational studies of the proton stopping power and water-equivalent parameters of tissue-equivalent and polymer-based materials in a unique way. The review also considers various evaluation measures, including relative stopping power (RSP), water-equivalent ratio (WER), and water-equivalent thickness (WET), thereby allowing studies that used varying methodologies to be appraised together. Also, incorporating studies that used established computational tools and reference databases provides additional criteria for assessing the consistency of the reported results. Several limitations should also be acknowledged. The substantial methodological and material heterogeneity among the included studies precluded a meaningful quantitative meta-analysis. Differences in proton energy ranges, material composition and density, experimental conditions, computational models, and definitions or calculation procedures for RSP, WER, and WET made direct numerical comparison between some studies inappropriate. In accordance with the nature of the available evidence, the findings were therefore synthesized qualitatively rather than statistically pooled. Furthermore, the number of available studies was not evenly distributed across all investigated materials, which may limit the strength of conclusions for less frequently studied tissue-equivalent and polymeric materials. Therefore, the findings of this review should be interpreted in the context of the specific material, proton energy range, and methodology used in each study.

6. Conclusion

This systematic review examined the published literature on determining the proton stopping power and water-equivalent properties of polymeric and tissue-equivalent materials used in proton therapy and proton dosimetry. It was observed that water is the primary reference material, and that PMMA, polyethylene, polystyrene, and other tissue-equivalent materials are useful for certain dosimetry and phantom applications once their relevant radiological characteristics are known .Proton stopping power was found to depend on the material's composition and density, the material's electron density, the proton energy, and the techniques used to determine it. Different techniques and methods such as experimental measurements, calculations, and Monte Carlo simulations, together with the NIST PSTAR and SRIM databases, can be complementary. Confidence in reported stopping power and water-equivalent properties can be improved by employing different approaches and supporting them with appropriate independent measurements .Among polymeric materials,

PMMA, polyethylene, and polystyrene have the best water-equivalent properties in proton dosimetry for certain applications over a given range of proton energies; therefore, most publications pertain to these polymeric materials. However, based on the reviewed literature, none of these polymeric materials can be assumed to be universally water-equivalent across all possible applications, material thicknesses, and proton energies. Hence, independent validation of computational materials characterization or experimentation is necessary for applications in which high-accuracy proton measurements are desired .Based on the current data, appropriately characterized tissue-equivalent and polymer materials are acceptable for use in proton therapy dosimetry, detector calibration, making phantoms, treatment plan verification, and quality assurance. In the future, studies should use more clearly defined techniques, and consistent techniques should be standardized across studies. This would also include reporting the composition of each material, its density, and the energy range for which proton stopping power is reported. It is also important to state the uncertainty of the measurement. These improvements would enable better validation of theoretical and Monte Carlo calculations and enhance the reliability of data on proton stopping power and water equivalence, leading to more accurate and reproducible applications in proton therapy.

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