GammaTile™:
A Novel Intraoperative Cesium-131 Collagen Tile Brachytherapy Device for the Treatment of Brain Tumors

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Group 5

NOTE

> May start reading:

- The role of GammaTile in the treatment of brain tumors: a technical and clinical overview
- First clinical implementation of GammaTile permanent brain implants after FDA clearance
- Comprehensive Commissioning and Clinical Implementation of GammaTiles STaRT for Intracranial Brain Cancer

OUTLINE

I. Introduction - **Rachelle**
   A. Background of Brain Tumor Management
      1. Challenges in management of recurrent and previously irradiated brain tumors
      2. Limitations of postoperative EBRT/SRS such as treatment delay, cavity dynamics, radionecrosis risk
   B. Evolution of Brain Brachytherapy
   C. Emergence of GammaTile Technology
   D. Rationale for using Cs-131

II. Overview of GammaTile Technology - **Rachelle**
   A. Device Composition
   B. Physical Design
   C. Mechanism of Action
   D. Advantages over Conventional Techniques
      1. Compared with EBRT/SRS
      2. Compared with traditional seed implants

III. Physics and Radioactive Properties of Cesium-131 - **Divs**
   A. Radionuclide Characteristics
      1. Physical Half-life
      2. Photon Energy Spectrum - mean photon energy, energy range
      3. Decay Characteristics - discuss electron capture decay and emission of low-energy x/gamma photons
      4. Dose Rate Characteristics - discuss high initial dose rate then rapid dose falloff, discuss dose delivery timeline (majority of dose delivered within weeks)
   B. Dosimetric Principles
      1. TG-43 Formalism - mention AAPM TG-43U1S2 implementation
      2. Seed Characteristics - IsoRay CS-1 Rev2, Air kerma strength, Seed geometry
      3. Prescription Parameters - ex. Approximate dose ~60 Gy at 5 mm depth
   C. Comparison with Other Isotopes used in Intracranial Brachytherapy
      1. Cs-131 vs I-125 (*compare: Half-life, Dose rate, Biologic effectiveness, Radionecrosis potential, Radiation protection implications*) - ie., shorter half-life, higher initial dose rate, lower prolonged radiation exposure
         ***May recreate this kind of table**

Property	Cs-131	I-125
Half-life	9.7 d	59.4 d
Mean energy	~30 keV	~28 keV
Dose delivery speed	Rapid	Slow
Implant duration	Shorter	Longer

   D. Dosimetric Advantages (ie., reduced hotspots, uniform cavity coverage, steep dose falloff)

IV. Radiobiologic Considerations - **Rendell**
   A. Tumor Cell Repopulation - *importance of immediate irradiation, rapid progression after surgery*
   B. Dose Rate Effects - *continuous low-dose-rate irradiation, biologic effect on residual microscopic disease*
   C. Spatial Dose Distribution - *sharp dose gradient, normal brain sparing*
   D. BED/EQD2 Distribution - *may present BED calculations, comparison with SRS regimens*

V. Treatment Planning and Clinical Workflow - **Nico**
   A. Multidisciplinary Collaboration - Neurosurgery, Radiation oncology, Medical physicist, Radiation safety officer
   B. Preoperative Planning - MRI-based cavity estimation, Determination of tile number and placement
   C. Intraoperative Workflow - Tumor resection, Lining cavity with GammaTiles, Correct tile orientation (textured side toward cavity), Fibrin sealant application
   D. Postimplant Evaluation - CT/MRI fusion, Seed localization, Dosimetric verification

VI. Radiation Protection and Safety - **RADTECHS**
   A. Radiation Safety Principles (ie., ALARA principles)
   B. Exposure Characteristics (low-energy photons, rapid decay)
   C. Regulatory Considerations
   D. Staff Protection
      1. OR staff (Minimize exposure, limit handling time)
      2. Role of Medical Physicist (Seed Handling, Surveys, Documentation)
   E. Exposure Rate Measurements
   F. Shielding Requirements (Lead HVL)
   G. Patient Instructions
   H. Waste and Source Accountability (Seed inventory, Documentation, Sterility and Disposal)

VII. Clinical Outcomes and Evidence - **Dexter**
   A. Overview of Indications and Clinical Outcomes - *may compare with other modalities such as postop SRS, whole brain RT, conventional brachytherapy*
      1. Brain Metastasis
      2. Glioblastoma
      3. Meningioma
   B. Safety Profile - acute and late toxicities
   C. Summary of Key Trials

VIII. Cost and Accessibility Considerations

IX. Future Directions

X. Conclusion

A. May summarize:
    1. Technical feasibility
    2. Favorable dosimetry
    3. Radiation safety profile
    4. Emerging efficacy data
    5. Future directions
B. Can be as simple as:
    1. GammaTile Cs-131 brachytherapy is a feasible and effective intraoperative radiation strategy
    2. Provides immediate, localized radiation with favorable dosimetry and manageable toxicity
    3. Particularly promising in recurrent and previously irradiated brain tumors
    4. Requires coordinated neurosurgical, radiation oncology, medical physics, and radiation safety support

- Suggested Figures
    a. Physics/Technical
        i. Cs-131 decay scheme
        ii. GammaTile structure diagram
        iii. Seed spacing illustration
        iv. Dose falloff graph
        v. TG-43 dose distribution
    b. Clinical
        i. Preoperative MRI
        ii. Intraoperative placement photo
        iii. Postimplant CT fusion
        iv. Isodose distribution
        v. Workflow diagram

- Suggested Tables
    a. Physical properties of Cs-131
    b. Comparison of radionuclides used in brain BT
    c. Clinical workflow roles
    d. Radiation safety recommendations
    e. Summary of published GammaTile studies
    f. Toxicity profile across studies

TIMELINE

- **May 08, 2026**
    - Discuss the working title, outline, and division of parts
- **May 09-10, 2026**
    - Do own reading and research on the topic
- **May 11-15, 2026**
    - Write paper, do initial edits
- **May 16-17, 2026**
    - Finalize paper, do PPT

I. Introduction

A. Background of Brain Tumor Management

Brain tumors are a heterogeneous group of neoplasms with variable histology, biologic behavior, prognosis, and treatment response. Their management often requires a multidisciplinary approach that includes maximal safe resection, external beam radiotherapy (EBRT), stereotactic radiosurgery (SRS), systemic therapy, and image-guided treatment planning. Despite these advances, local recurrence remains a major clinical challenge, particularly in brain metastases, glioblastoma, and recurrent or aggressive meningiomas. Although surgery can relieve mass effect, establish diagnosis, and reduce gross disease burden, microscopic residual disease may persist along the operative bed and later contribute to local failure. As a result, adjuvant radiation therapy remains central to postoperative management, but durable local control remains difficult in selected postoperative and previously treated tumors [1].

Postoperative EBRT and SRS typically require an interval after surgery to allow adequate wound healing, clinical recovery, postoperative imaging, simulation, and treatment planning. While this interval supports safe and accurate treatment delivery, residual tumor cells may proliferate during this period before adjuvant radiation is initiated. In addition, postoperative cavity dynamics may complicate target delineation because the resection cavity can change in size, shape, and position between surgery, planning, and treatment delivery. These issues are particularly relevant for highly conformal techniques such as SRS, where accurate cavity definition is essential to balance local control with normal brain toxicity [1,2].

Management of recurrent or previously irradiated brain tumors is challenging. In these settings, repeat EBRT or SRS may be limited by cumulative normal brain tolerance and the risk of adverse radiation effects, including edema and radiation necrosis. These challenges have renewed interest in intraoperative radiation strategies that can deliver treatment directly to the surgical bed while minimizing dose to uninvolved brain tissue [1,2].

B. Evolution of Brain Brachytherapy

Intracranial brachytherapy provides a method of delivering radiation directly to the tumor bed or postoperative cavity. By placing radioactive sources within or adjacent to the operative bed, brachytherapy can deliver a high localized dose to tissue at greatest risk for microscopic residual disease, while the rapid spatial dose fall-off reduces exposure to the surrounding normal brain [1].

Earlier intracranial brachytherapy techniques included permanent seed implants, including stranded seed techniques in which radioactive seeds were arranged in linear strands along the resection cavity. Although these methods demonstrated feasibility of immediate postoperative radiation delivery, they were limited by practical and dosimetric challenges, including irregular seed spacing, possible direct seed-to-brain contact, source migration, and dose heterogeneity. These limitations could create high-dose “hot spots” or underdosed “cold spots,” potentially affecting both tumor control and toxicity [1,3].

C. Emergence of GammaTile™ Technology

GammaTile™ is a surgically targeted radiation therapy platform developed to address some of the limitations of conventional postoperative radiation and traditional seed-based brachytherapy. The device consists of cesium-131 radioactive seeds embedded within a bioresorbable collagen tile. After tumor resection, the tiles are placed along the surfaces of the operative cavity considered at risk for recurrence, allowing radiation to begin immediately after surgery [1,3].

GammaTile received United States Food and Drug Administration clearance in 2018 for recurrent brain tumors, with expanded clearance in 2020 for upfront use in newly diagnosed malignant brain tumors. Since its introduction, published reports have described its technical design, workflow, dosimetry, radiation safety, and clinical outcomes in brain metastases, glioblastoma, and meningioma [1].

The clinical rationale for GammaTile centers on two major barriers in postoperative brain tumor management: delay to adjuvant radiation and difficulty treating recurrent tumors in previously irradiated tissue. By placing radioactive sources directly into the resection cavity at surgery, GammaTile eliminates the waiting period between surgery and radiotherapy. By using low-energy Cs-131 sources, it also delivers a high localized dose near the cavity surface with steep dose fall-off into the surrounding brain [1,3].

D. Rationale for Using Cesium-131

Cesium-131 is well suited for permanent intracranial brachytherapy because of its low photon energy and relatively short physical half-life of approximately 9.7 days. Compared with iodine-125, which has a longer half-life of approximately 59.4 days, Cs-131 delivers radiation over a shorter period and at a higher initial dose rate. This may be advantageous in aggressive tumors where residual microscopic disease can repopulate soon after surgery [1,3].

The rapid decay of Cs-131 also complements the GammaTile platform. Dosimetric modeling suggests that collagen tile brachytherapy limits clinically significant source migration and maintains dose delivery during the period when most of the Cs-131 dose is deposited [4]. Thus, GammaTile combines immediate intraoperative radiation delivery, standardized source geometry, controlled seed-to-brain spacing, and rapid Cs-131 dose deposition into a single implantable device.

II. Objectives

General Objective

The general objective of the case study is to review the technical, radiobiologic, dosimetric, radiation safety, and clinical aspects of GammaTile cesium-131 (Cs-131) implant brachytherapy in the management of brain tumors.

Specific Objectives

Specifically, this case study aims to:

1. To describe the physical, radioactive, and radiobiologic properties of Cs-131 relevant to intracranial brachytherapy.
2. To discuss the treatment planning process, dosimetric principles, and multidisciplinary workflow involved in GammaTile implantation.
3. To review radiation protection and safety considerations associated with GammaTile Cs-131 brachytherapy.
4. To evaluate current evidence on the efficacy and safety of GammaTile therapy in the management of brain tumors.
5. To identify the advantages and limitations of GammaTile Cs-131 brachytherapy in contemporary neuro-oncology practice.

III. Overview of GammaTile™ Technology

A. Device Composition

GammaTile™ is a permanently implanted, bioresorbable collagen tile containing cesium-131 radioactive seeds. Each tile contains four titanium-encapsulated Cs-131 seeds embedded within a collagen matrix. The collagen component functions as both a source carrier and a spacer,

maintaining a fixed relationship between the radioactive seeds and the adjacent brain surface [1,3].

The collagen matrix is similar to material used in neurosurgical reconstruction and dural repair. It is relatively rigid when dry, facilitating intraoperative handling, and becomes flexible when hydrated, allowing it to conform to the complex surfaces of a resection cavity. Multiple tiles can be placed adjacent to one another to cover the operative bed at risk for recurrence [3].

B. Physical Design

Each GammaTile measures approximately 20 × 20 × 4 mm and contains four Cs-131 seeds arranged in a fixed geometry. The seeds are spaced approximately 10 mm apart and are offset approximately 3 mm from the surface of the tile that faces the operative bed or brain parenchyma. The 10-mm interseed spacing is intended to reduce hot and cold spots caused by irregular seed placement, while the 3-mm offset prevents direct seed-to-brain contact and reduces excessive focal dose to the tissue surface [1,3].

GammaTile has a smooth surface and a textured surface. During implantation, the textured surface is oriented toward the operative bed because this orientation provides the intended seed-to-brain offset. Correct tile orientation is therefore important for achieving the intended dose distribution [1,3].

C. Mechanism of Action

After maximal safe resection, GammaTiles are placed along the surfaces of the surgical cavity judged to be at risk for microscopic residual disease. Once implanted, the Cs-131 seeds immediately begin delivering continuous low-dose-rate radiation to adjacent tissue. Because the radioactive sources are positioned directly along the operative cavity, the highest dose is delivered near the cavity surface, with steep dose fall-off into the surrounding normal brain [1].

The GammaTile design and source strength produce a physical dose of approximately 60 Gy to a depth of 5 mm in the brain, although the final dose distribution depends on cavity size, cavity shape, number of tiles, and implant configuration [1]. This allows focused treatment of the high-risk surgical margin while reducing dose to more distant normal brain tissue.

D. Advantages Over Conventional Techniques

1. Compared with EBRT/SRS

The advantage of GammaTile over postoperative EBRT or SRS is immediate radiation delivery. Conventional postoperative radiation is commonly delayed by wound healing, recovery, imaging, simulation, and planning. GammaTile begins delivering radiation at the time of tumor resection, potentially reducing the opportunity for early tumor cell repopulation before adjuvant therapy [1,3].

GammaTile may also reduce the impact of postoperative cavity dynamics. With EBRT or SRS, the target volume is defined after surgery, and the cavity may change between imaging, planning, and treatment delivery. In contrast, GammaTile is placed directly on the operative bed at surgery. Its low-energy intracavitary radiation also produces steep dose fall-off, concentrating dose near the high-risk cavity surface while limiting exposure to more distant normal brain [1,2].

2. Compared with Traditional Seed Implants

Compared with traditional permanent seed or stranded seed implants, GammaTile provides a more standardized and reproducible implant geometry. The collagen matrix fixes the Cs-131

seeds in position, preserving consistent interseed spacing and reducing the likelihood of irregular high- or low-dose regions [1,3].

The tile also functions as a spacer by maintaining a built-in offset between the radioactive seeds and the brain surface. This avoids direct seed-to-brain contact and helps reduce excessive focal dose at the operative bed. In addition, the modular tile structure allows simpler and faster intraoperative placement than individually arranging multiple free or stranded seeds along the surgical cavity [3,5].

Overall, GammaTile™ represents an evolution in intracranial brachytherapy by combining immediate intraoperative radiation delivery, standardized Cs-131 seed geometry, a bioresorbable collagen carrier, and localized dose fall-off. These features support its role as a novel adjuvant radiation strategy for selected resected brain tumors, particularly in recurrent or previously irradiated settings.

IV. Physics and Radioactive Properties of Cesium-131

A. Radionuclide Characteristics

1. Physical Half-life
2. Photon Energy Spectrum
3. Decay Characteristics
4. Dose Rate Characteristics

B. Dosimetric Principles

C. Comparison with Other Isotopes used in Intracranial Brachytherapy

D. Dosimetric Advantages

V. Radiobiologic Considerations

The radiobiologic rationale for cesium-131 (Cs-131) intracavitary brachytherapy is largely based on its ability to deliver a high biologically effective dose to microscopic residual disease immediately following surgical resection while minimizing irradiation of surrounding normal brain tissue. In contrast to postoperative external beam radiation therapy (EBRT), which is commonly delayed for wound healing and treatment planning, GammaTile implantation initiates radiation delivery at the time of surgery. This is particularly relevant in aggressive intracranial tumors such as glioblastoma and metastatic disease, where rapid postoperative repopulation and early local recurrence have been documented [1].

Cs-131 possesses favorable radiobiologic characteristics for intracranial brachytherapy because of its relatively short physical half-life and higher initial dose rate compared with iodine-125. The majority of the prescribed dose is delivered within the first month after implantation, allowing treatment to coincide with the period of highest tumor cell proliferative activity following resection. Rapid dose delivery may also reduce the opportunity for accelerated tumor repopulation while limiting prolonged low-dose radiation exposure to adjacent normal tissues [3].

Another important radiobiologic advantage of Cs-131 brachytherapy is the steep dose gradient generated by its low-energy photon emissions. This permits delivery of high radiation doses immediately adjacent to the resection cavity while achieving rapid dose falloff within surrounding brain parenchyma. Such spatial dose distribution is particularly advantageous in previously irradiated tumors, where cumulative radiation tolerance of normal brain tissue remains a major concern. Compared with EBRT or repeat stereotactic radiosurgery, intracavitary Cs-131

implants may therefore improve local control while potentially reducing the risk of symptomatic radiation necrosis [1].

The GammaTile platform also addresses several limitations historically associated with intracranial brachytherapy. The fixed inter-seed spacing and standardized 3 mm offset from the brain surface promote more homogeneous dose distribution and reduce focal overdosing at the tissue interface. These design characteristics may contribute to lower rates of radiation-related toxicity while maintaining effective irradiation of infiltrative microscopic disease along the surgical cavity margin.

VII. Treatment Planning and Clinical Workflow

A. Multidisciplinary Collaboration

Treatment planning and implementation of GammaTile surgically targeted radiation therapy (STaRT) require close multidisciplinary coordination among neurosurgery, radiation oncology, medical physics, and radiation safety personnel. Successful program implementation depends on collaborative preoperative planning, intraoperative execution, and postoperative dosimetric assessment to ensure accurate source placement, optimal target coverage, and adherence to radiation safety standards. Ferreira et al. emphasized that commissioning of a GammaTile program necessitates coordinated involvement of the neurosurgeon, radiation oncologist, medical physicist, and radiation safety officer, particularly in protocol development, dosimetric verification, source accountability, and patient release procedures [3].

B. Preoperative Planning

Preoperative planning is primarily based on contrast-enhanced magnetic resonance imaging (MRI), which is used to estimate the anticipated postoperative resection cavity and determine the number of GammaTiles required for adequate cavity coverage. The gross tumor volume is delineated preoperatively, and the estimated cavity surface area at risk for recurrence is calculated while accounting for expected intraoperative cavity contraction and non-target surfaces such as the skull interface. The required number of tiles is subsequently estimated by dividing the anticipated treatment area by the surface area of each GammaTile. This process is performed collaboratively by the neurosurgeon, radiation oncologist, and medical physicist [3].

C. Intraoperative Workflow

During surgery, GammaTiles are implanted immediately following maximal safe tumor resection. The neurosurgeon lines the operative cavity with sufficient tiles to cover regions considered at highest risk for local recurrence, particularly the brain parenchyma adjacent to the resection bed. Proper orientation of the implant is essential, with the textured surface of the collagen tile positioned toward the cavity wall to maintain the intended 3 mm offset between the cesium-131 seeds and the brain surface. This offset reduces excessive focal dose deposition while preserving conformability to the surgical cavity. The tiles are then secured using fibrin sealants or adhesive fibrin glue to stabilize the implant and fill the resection cavity [3].

D. Postimplant Evaluation

Postimplant evaluation involves imaging-based verification of seed position and dosimetric assessment. Following surgical closure, thin-slice non-contrast computed tomography (CT) is typically obtained and fused with postoperative MRI for accurate seed localization and evaluation of implant geometry. Postimplant dosimetric analysis is subsequently performed using treatment planning systems based on TG-43 formalism to confirm source distribution and radiation dose coverage. Ferreira et al. reported that treatment planning system commissioning and dose validation were performed using consensus dosimetric parameters from the AAPM TG-43U1S2 recommendations for Cs-131 sources [3].

VIII. Radiation Protection and Safety

A. Radiation Safety Principles

GammaTile® therapy is designed to deliver highly conformal radiation treatment to the postoperative resection cavity while minimizing exposure to surrounding normal tissues and healthcare personnel. The device consists of low-energy cesium-131 (Cs-131) seeds embedded within a bioresorbable collagen tile, producing a steep dose gradient due to the radionuclide's mean photon energy of approximately 30.4 keV. This rapid dose fall-off substantially limits radiation exposure beyond the target volume and supports the principle of keeping radiation exposure "as low as reasonably achievable" (ALARA) [1,3,5,6].

GammaTile implants are designed to deliver a high dose immediately adjacent to the surgical cavity while limiting exposure to deeper brain structures. Clinical implementation studies have reported prescription doses of approximately 60 Gy at 5 mm depth, allowing effective treatment of microscopic residual disease while reducing irradiation of uninvolved tissue. The low photon energy of Cs-131 results in rapid attenuation within tissue, thereby sparing nearby critical structures and scalp from significant radiation exposure [1,3,4,5].

1. Immediate, Localized Dosing

An important advantage of GammaTile therapy is the immediate initiation of radiation treatment at the time of surgery. Unlike postoperative external beam radiotherapy, which may require several weeks before treatment initiation, GammaTile begins delivering therapeutic radiation intraoperatively, thereby avoiding delays associated with wound healing or treatment planning. This approach also eliminates the need for multiple outpatient radiation fractions, reducing cumulative exposure opportunities for patients and staff [1,3,10,27].

2. Short Half-life, Quick Dose Recovery

The short physical half-life of Cs-131 enables rapid dose delivery, with approximately 88%–90% of the prescribed dose delivered within the first month after implantation. Compared with longer-lived isotopes such as iodine-125, Cs-131 substantially reduces the duration of residual radioactivity and minimizes prolonged radiation exposure to surrounding tissues, caregivers, and healthcare workers [1,4,6,7].

3. Collagen Offset Reduces Hotspots

The collagen carrier within the GammaTile device further contributes to dose optimization and safety. Each seed is positioned approximately 3 mm from the tissue surface, reducing focal dose hotspots at the brain interface while maintaining adequate target coverage. In addition, the fixed spacing of the seeds within the tile promotes a predictable and homogeneous dose distribution and decreases the likelihood of seed clustering [1,4,5].

4. Pre-planning and Team Collaboration

Safe implementation of GammaTile therapy also relies on coordinated multidisciplinary planning involving neurosurgery, radiation oncology, medical physics, and radiation safety personnel. Preloaded and sterilized tiles are manufactured according to preoperative cavity estimates, thereby minimizing intraoperative manipulation of radioactive material. This streamlined workflow reduces handling time and limits occupational exposure. Measured exposure rates to staff during implantation have been reported to be very low, supporting the safety of the procedure when standard radiation precautions are followed [3,5,15].

5. Avoidance of Reirradiation

Because GammaTile delivers the prescribed radiation dose during a single surgical procedure, repeat brachytherapy procedures and additional radiation sessions are often avoided. This one-time implantation approach further limits cumulative radiation exposure and aligns with ALARA principles by minimizing unnecessary irradiation to patients, staff, and caregivers. Overall, the combination of localized dose delivery, rapid radioactive decay, optimized tile geometry, and efficient procedural workflow makes GammaTile a brachytherapy platform inherently designed around radiation safety principles [1,6,10].

B. Exposure Characteristics

GammaTile devices contain four titanium-encapsulated Cs-131 seeds within a 20 × 20 × 4 mm collagen matrix. Cs-131 decays via electron capture, emitting low-energy photons with a short physical half-life [1,4,5,6].

The low photon energy results in rapid tissue attenuation and steep dose fall-off, confining most absorbed dose to the surgical cavity with minimal exposure to surrounding brain and distant tissues. The fixed geometry ensures predictable dosimetry and reduces seed displacement risk. The lead half-value layer (HVL) for Cs-131 is approximately 0.025 mm, indicating that only minimal shielding is required to attenuate emitted radiation effectively. Thin lead barriers or standard radiation-protective materials, therefore, provide substantial attenuation of Cs-131 emissions [1,5,6].

In addition, the fixed spacing of the seeds within the collagen matrix promotes uniform dose distribution and reduces the risk of seed migration. The titanium encapsulation surrounding each seed provides secure containment of radioactive material and prevents leakage during implantation and long-term placement. Collectively, the low-energy emissions, short half-life, and localized dose deposition of Cs-131 make GammaTile a highly conformal form of intracranial brachytherapy with limited shielding requirements relative to higher-energy radionuclide sources [4,5,6].

C. Regulatory Considerations

The clinical use of GammaTile is governed by national and international regulations pertaining to sealed radioactive sources and medical use of byproduct material. Cs-131 seeds may only be possessed, stored, and implanted by licensed institutions and authorized personnel operating under established radiation safety programs. Strict source accountability is required throughout receipt, storage, implantation, transfer, and disposal processes [12,13,14,16].

Facilities using GammaTile must maintain detailed inventory records documenting seed serial numbers, activity, receipt dates, implantation records, transfer information, and disposal documentation. Any missing or unaccounted radioactive source must be immediately reported to the appropriate regulatory authority in accordance with institutional and governmental requirements [12,14].

Routine radiation safety procedures include leak testing of sealed Cs-131 sources to confirm removable contamination remains below 0.005 μCi per seed. Personnel involved in handling GammaTile devices must receive appropriate radiation safety training and adhere to ALARA principles emphasizing minimization of exposure through time, distance, and shielding [12,14,15].

Patient release following implantation must comply with applicable public dose limits, including those outlined in 10 CFR 35.75 and related NCRP and IAEA guidance documents. Before discharge, patient-specific assessments are performed to verify that radiation exposure to family

members, caregivers, and the public is unlikely to exceed recommended dose constraints, typically <5 mSv. Written radiation safety instructions are provided whenever clinically indicated [7,12,13,14].

Unused, damaged, or contaminated Cs-131 sources must be managed as radioactive material and disposed of in accordance with institutional policies and applicable regulatory requirements. Comprehensive documentation of inventories, leak tests, radiation surveys, patient release calculations, and disposal records must be retained for regulatory compliance and audit purposes [12,14].

D. Staff Protection

Operating room personnel involved in GammaTile implantation should minimize time near active sources and maximize distance whenever feasible. Because Cs-131 emits low-energy photons, even minimal shielding and short distances provide substantial dose reduction. A lead thickness of approximately 0.25 mm attenuates nearly all Cs-131 emissions, making standard lead barriers and surgical shielding materials highly effective [1,3,5].

All personnel handling radioactive implants should wear appropriate dosimetry, including whole-body and extremity dosimeters, to verify occupational exposures remain within regulatory limits. Published reports have demonstrated very low occupational exposure rates associated with GammaTile implantation, supporting the safety of the procedure when appropriate radiation precautions are observed [5,12,14].

Intraoperative handling protocols emphasize the use of forceps and shielded barriers to minimize direct contact with radioactive material. Tiles should never be manipulated with bare hands, and any dropped or damaged seed must be isolated immediately and managed according to institutional spill and contamination procedures [5,12].

The medical physicist plays a central role in GammaTile safety and quality assurance. Responsibilities include commissioning the treatment planning system, validating Cs-131 source parameters according to AAPM TG-43 formalism, verifying source strength, performing radiation surveys, and documenting implant activity and source accountability. Independent dose verification and periodic review of personnel dosimetry are also essential components of the safety program [5,15].

Comprehensive documentation must be maintained throughout the implantation process, including shipment records, inventory logs, leak-test certificates, patient implant records, and radiation survey data. Institutional emergency procedures should also address management of damaged sources, contamination events, and source recovery.

E. Exposure Rate Measurements

1. Initial Dose Rates

Post-implant exposure rate measurements are an essential component of radiation safety evaluation following GammaTile implantation. Published clinical series have demonstrated relatively low exposure rates associated with Cs-131 brain implants. Reported median exposure rates immediately after implantation were approximately 1.2 mSv/h at contact, 0.08 mSv/h at 30 cm, and 0.01 mSv/h at 1 m from the implant site.

2. Time Dependence

Because Cs-131 has a physical half-life of 9.69 days, exposure rates decrease rapidly over time according to radioactive decay principles. Approximately 90% of the total prescribed dose is delivered within the first month after implantation.

3. Instrument Sensitivity
A thin-window detector is essential for accurate measurements. Standard survey meters with thicker housings can significantly underestimate exposure from the ~30 keV photons emitted by Cs-131. Using thin mica or aluminum windows—or operating an ion chamber with its window removed—allows most low-energy photons to reach the sensitive volume of the detector. Hospital radiation safety guidance similarly recommends thin-window probes for low-energy photon surveys. By opening the chamber window to full sensitivity, the need for additional correction factors is effectively eliminated.

4. Measurement Procedure
Exposure surveys are typically performed within 24–48 hours after surgery by a qualified medical physicist or trained radiation safety personnel. Standard measurement distances include direct scalp contact, 30 cm, and 100 cm from the implant site. An ionization chamber survey meter with the window open/removed (e.g., Fluke 451B) or a thin-window Geiger–Müller probe is used to avoid attenuation of ~30 keV photons. Instruments are calibrated for Cs-131 per US NRC or AAPM standards, typically annually, with ±20% accuracy. At low dose rates, care is taken to ensure the detector response remains within its reliable operating range without saturation. All survey results, including date, instrument identification, and measured values, are documented in compliance with 10 CFR 35.2404.

These measurements are used to guide radiation safety protocols. The physicist uses the recorded dose rates to estimate precaution times and prepare discharge instructions, typically based on NRC Reg. Guide 8.39 or NCRP guidance, ensuring exposures remain within regulatory limits. For example, modeled estimates show <1 mSv to family members and ~0.06 mSv to care teams, both well below US annual limits (5 mSv for caregivers and 50 mSv occupationally). Measured dose rates, often at 30 cm, are grouped into ranges that determine recommended contact restrictions, with longer precautions for pregnant individuals and children.

5. Shielding Factor
The patient's skull and surrounding tissues provide substantial attenuation of emitted radiation. One reported shielding factor—defined as the ratio of dose rate from an equivalent unshielded point source to the measured dose rate at 1 meter—was approximately 9.4. In clinical settings, variations in implant depth and cranial bone thickness are expected, but a reduction on the order of magnitude is generally observed. This parameter is useful for estimating caregiver exposure and for validating measured values against dosimetric prediction models.

6. Documentation
Measured exposure rates are used to guide patient-release instructions and caregiver precautions in accordance with regulatory recommendations. Documentation of survey results, instrumentation, decay corrections, and patient-release calculations must be maintained in the medical record and radiation safety log as required by regulatory standards.

F. Shielding Requirements
Because Cs-131 emits low-energy photons with a mean energy of approximately 30 keV, shielding requirements for GammaTile implants are minimal. The lead HVL for Cs-131 is approximately 0.025 mm; therefore, thin lead barriers provide substantial attenuation. Standard 0.5 mm lead aprons effectively attenuate nearly all Cs-131 emissions.

In clinical practice, staff protection relies primarily on minimizing handling time and maximizing distance from the implant site rather than using heavy shielding. Placing any lead barrier (e.g. a 0.5-mm lead surgical drape or a sterile lead sheet) between the active tile and staff provides effective protection. Even modest increases in distance substantially reduce exposure because of the inverse square law. Measured exposure rates fall sharply with increasing distance, with values decreasing from approximately 0.08 mSv/hr at 30 cm from a Cs-131 implant to about 0.01 mSv/hr at 1 meter.

Patient tissues also provide significant self-shielding, as the skull and overlying soft tissues absorb a large proportion of the emitted low-energy photons. This additional attenuation further limits exposure to operating room personnel, caregivers, and the public.

Unused GammaTile implants are stored and transported in manufacturer-provided shielded containers. Owing to the low photon energy and minimal HVL of Cs-131, no extensive structural shielding is required for routine storage and handling.

G. Patient Instructions

Patients undergoing GammaTile implantation should receive pre-admission counseling regarding the surgical procedure, radiation safety considerations, expected hospitalization, and postoperative care requirements. Counseling includes discussion of the purpose of Cs-131 brachytherapy, anticipated benefits and risks, postoperative recovery expectations, and temporary radiation precautions after discharge. Standard preoperative instructions include fasting requirements, medication review, pregnancy assessment when applicable, laboratory evaluation, and anesthesia clearance.

Before discharge, patients and caregivers should receive individualized verbal and written radiation safety instructions based on patient-specific dose assessments. Patient release is permitted only when projected radiation exposure to another individual is not expected to exceed regulatory dose limits. Written instructions are recommended when projected exposure to another person may exceed 1 mSv.

Discharge instructions may include temporary limitations on prolonged close contact with young children or pregnant individuals, depending on measured exposure rates and calculated occupancy factors. Patients should also be advised that routine contact does not make clothing, bedding, or bodily fluids radioactive because the Cs-131 sources remain sealed within the implanted device.

Patients must be instructed not to manipulate the surgical site and to notify the treating team immediately if wound disruption or suspected implant displacement occurs. In addition, patients are advised to carry implant identification documentation and inform healthcare providers before undergoing MRI examinations or other procedures. MRI scanning may be performed only under the MR-conditional specifications outlined in the manufacturer’s Instructions for Use.

H. Storage, Transport, Waste Management, and Source Accountability

Strict source accountability measures must be maintained throughout the receipt, storage, transport, clinical use, and disposal of GammaTile implants containing Cs-131 seeds. Upon receipt, shipments should be verified by the authorized medical physicist using manufacturer documentation that includes source activity, lot numbers, reference dates, and certification records. All receipt and inventory activities must be documented to ensure continuous source tracking.

GammaTile implants and any associated radioactive materials should be stored in locked, shielded, designated areas accessible only to authorized personnel. Standard ALARA precautions, including minimizing handling time, maximizing distance, and using shielding and forceps when appropriate, must be consistently applied during all handling procedures.

Before implantation, the medical physicist verifies source count and activity, after which the implants are transported to the operating room in shielded and properly labeled containers using documented chain-of-custody procedures. During implantation, aseptic handling techniques are maintained in accordance with the manufacturer's Instructions for Use.

Immediately before and after implantation, source reconciliation and radiation surveys are performed to confirm complete accountability of all radioactive material. Implanted seeds are documented within the patient treatment record. Since the Cs-131 seeds remain permanently implanted and the collagen matrix gradually bioresorbs, routine surgical waste generated during the procedure is generally non-radioactive.

Unused, damaged, or suspect radioactive sources must be isolated and managed according to institutional radiation safety procedures and regulatory requirements. Such materials should never be discarded in standard waste streams and must instead be returned to the manufacturer or processed through approved radioactive waste disposal pathways. In cases involving source damage, contamination, or suspected source loss, radiation safety personnel should immediately initiate emergency response procedures, including area restriction, contamination surveys, and source recovery measures.

Comprehensive documentation—including inventory records, survey results, transfer logs, implantation records, and disposal documentation—must be maintained to ensure compliance with institutional policy, regulatory requirements, and international radiation safety guidance.

VIII. Clinical Outcomes and Evidence

GammaTile™ was initially cleared by the US FDA for recurrent brain tumors in 2018, and was subsequently approved for newly diagnosed brain tumors in 2020. Currently, it is being used in a wide variety of clinical scenarios, involving both newly diagnosed and recurrent malignant neoplasms in the central nervous system. Prospective randomized clinical trials are continuously ongoing, to establish the use of GammaTile™. Either as part of standard of care, or as adjunct to the current treatment options. This discussion will focus on its utility in brain metastases and glioblastoma.

A. Brain Metastases

Intracranial neoplasms secondary to metastasis from a known extracranial primary are a common complication of cancer, and are the most common type of brain tumors. The current standard of care for brain metastases is surgery whenever operable, followed by some form of radiation to the brain. This was established by the landmark Patchell studies, wherein the first Patchell study showed that addition of surgery to whole brain radiotherapy (WBRT) had better local control (80% vs 48%) and median overall survival (40 weeks vs 15 weeks) compared to whole brain radiotherapy alone (Patchell et al., 1990). Meanwhile the second Patchell study showed that for patients with solitary brain metastasis who underwent complete resection, addition of WBRT had increased local control (90% vs 54%) compared to surgery alone, but without significant difference in median overall survival (Patchell et al., 1998).

With the recent technological advances in radiation therapy techniques, a shift to delivering a more focal radiation to the brain has been observed. Since radiation to the whole brain may lead to increased cognitive impairment, as early as 3-6 months post-treatment. The NCCTG N107C/CEC.3 or RTOG 1270 trial compared stereotactic radiosurgery (SRS) and whole brain radiotherapy (WBRT) in the postoperative setting. In this prospective phase 3 study, they included patients with 1 resected brain lesion and randomized to either postoperative SRS (12-20 Gy in 1 fraction, with dose determined by surgical cavity volume) or WBRT (30 Gy in 10 fractions, or 37.5 Gy in 15 fractions). Cognitive-deterioration-free survival was longer (3.7 months vs 3 months; $p<0.001$) and cognitive deterioration at 6 months was less frequent (52% vs 85%; $p<0.0031$) in patients treated with SRS. Meanwhile, there is no significant difference in overall survival (12.2 months vs 11.6 months; $p<0.70$) between two modalities (Brown et al., 2017). A post-hoc central imaging review was done in this cohort (Breen et al., 2022), and determined that postoperative SRS was not significantly associated with lower rates of 12 month-local control compared with WBRT (79.2% vs 86.9%; $p=0.099$). This study showed that with maintained overall survival benefit and superior cognitive quality of life, postoperative SRS should be considered as one of the standards of care in this patient population.

One caveat of the RTOG 1270 trial was that although there is no statistically significant difference, there is a trend towards lower local control with postoperative SRS. This finding was contrary to conventional theory that SRS should result in superior local control due to its higher Biological Effective Dose. The mentioned posthoc analysis also showed that there is higher risk of local failure for patients with resection cavities > 3 cm and subsequently larger target volumes (Breen et al., 2022). It is unclear whether this is related to cavity size, cavity dynamics, tumor biology, or radiation dose. Another concern is the logistics and practicality of postoperative SRS. Ideally this adjuvant treatment should be delivered 3-4 weeks after surgery, to allow time for adequate wound healing. Some allow up to 8 weeks, to allow for rehabilitation and recovery from previous surgery. But a significant number of patients do not receive postoperative SRS within the recommended period. This was shown in one real-world analysis study in the US (Roth O'Brien et al., 2021), where around 33.33% of patients received postoperative SRS more than 8 weeks, or not at all. This cohort was associated with 48.5-50.0% local recurrence. Most common reasons cited in this study regarding interval to postoperative SRS > 4 weeks are: logistics (33.0%); treatment of primary or systemic disease (22.6%); and management of comorbidities (13.0%). This specific subset at risk for delayed/inability to receive adjuvant treatment poses a therapeutic challenge, as well as an opportunity for the use of GammaTile™ in the immediate postoperative setting.

There is an ongoing effort to acquire real-world data with the use cases of GammaTile™. The Surgically Targeted Radiation Therapy (STaRT) Registry is a multicenter prospective observational study, which involved up to 50 centers in the US. This registry enrolls all patients who received GammaTile™, and the following data were obtained: local control, overall survival, adverse events, quality of life. Patient accrual started last September 2020, and around 500 patients have been enrolled as of September 2025. The study completion is scheduled by 2028, and is estimated to enroll around 600 patients (GT Medical Technologies, Inc., 2026).

Preliminary study of patients with newly diagnosed brain metastases from the STaRT Registry was done (Zeller et al., 2024). Early experience with use of GammaTile™ showed 21.4% attributed adverse events, and 3.6% rate of serious adverse events within the 90 days from the tile placement. In the immediate postoperative period, 2 patients reported headache and pain, while 1 patient reported seizures requiring medication. At 1 month follow-up, there was 1 patient with reported superficial wound infection requiring surgical intervention without tile explantation. At 3 months follow-up, 1 patient reported facial pain not requiring any treatment. There was no

observed symptomatic hematoma. There is no observed increase in rates of local toxicity as a result of this procedure compared to historical controls with surgical resection, showing the safety of GammaTile™.

Another preliminary study of patients from the STaRT Registry was done to determine the efficacy of GammaTile™ in the setting of newly diagnosed brain metastases (Kite et al., 2026). Of the 51 patients included with median follow-up of 12.4 months, only 4 patients developed postoperative leptomeningeal disease (7.8%). The cohort showed 92.3% 1-year local control, 88.5% 1-year freedom from leptomeningeal disease, and 49% 1-year overall survival with the use of GammaTile™. In terms of adverse events, there is overall low incidence of wound infection (3.9%), cerebral edema (3.9%), and postoperative hemiparesis (1.9%). This is within what can be expected for the normal postoperative natural history for these patients. There is also no symptomatic radionecrosis observed from this cohort. Putting the results of this study into context, GammaTile™ showed higher 1-year local control rates (92.3%) compared to SRS (72%) published from the M.D. Anderson Cancer Center experience (Mahajan et al., 2017), although this is not a head-to-head comparison.

As of date, there is no published data directly comparing postoperative stereotactic radiosurgery/stereotactic radiotherapy (SRS/SRT) with Surgically Targeted Radiation Therapy (STaRT) using GammaTile™. There is currently an ongoing Phase 3 randomized control trial comparing these modalities, named ROADS (Radiation One And Done Study). The study has finished accrual, and interim results were presented in abstract form at the 2025 Congress of Neurologic Surgeons Annual Meeting (Agarwhal, 2026). Preliminary data showed that GammaTile™ is significantly superior in terms of surgical bed recurrence-free survival (HR: 0.42, p=0.0024) and time to recurrence (HR: 0.13, p=0.01). Final analysis and published manuscript is expected to be available this year.

B. Glioblastoma

Glioblastoma (GBM) is the most common primary intracranial neoplasm in adults. This disease has an aggressive course, and has poor prognosis. The current standard of care for GBM is maximally safe surgical resection followed by postoperative chemoradiation (60 Gy in 30 fractions, plus concurrent daily temozolamide) then adjuvant temozolamide alone for 6 cycles, also known as the Stupp protocol. This is based from the landmark EORTC-NCIC trial by Stupp et al. (2005) wherein for patients with newly diagnosed GBM (majority underwent resection, 84%), addition of temozolamide with radiotherapy followed by maintenance temozolamide increased median survival (14.6 months vs 12 months) and 2-year overall survival (26.5% vs 10.5%) compared to adjuvant radiotherapy alone. Long term follow-up was done (Stupp et al., 2009), wherein overall survival benefit at 5 years was maintained with addition of temozolamide (9.8% vs 1.9%). Despite increased survival with treatment optimization, these studies show dismal survival outcomes reflecting the severity of this disease.

Postoperative chemoradiation is ideally given 3-4 weeks (up to 6 weeks) after the initial surgery, to allow for adequate wound healing and sufficient patient recovery. Although it is documented that median time to recurrence after postoperative adjuvant therapy is around 7 months, the first evidence of tumor progression after surgery occurs prior to initiating postoperative chemoradiation. This first and initial tumor progression in the time interval between surgery and postoperative therapy is referred to as Rapid Early Progression (REP). A meta-analysis by Waqar et al. (2022) showed mean incidence of REP of 45.9% in the 9 studies included. REP is a strongly negative prognostic factor, and was associated with lower overall survival, lower progression-free survival, patients with subtotal resection, and patients with IDH wild-type tumors. REP may have further implications in the treatment of GBM. It could indicate a subset of

patients with intrinsically more aggressive tumors that may benefit from more intensified upfront therapy. It also presents an opportunity for the utility of GammaTile™ in this particular clinical scenario.

As most treatment failures in newly-diagnosed GBM patients are local, improving local control could potentially improve overall survival of these patients. To determine the feasibility and tolerability of adding GammaTile™ as an upfront boost at the time of maximal safe resection together with the backbone of standard of care approach, the GESTALT (GammaTile™ Enhanced Stupp Alternative) trial was initiated (GT Medical Technologies, Inc., 2025). Patient accrual was completed, and interim analysis was conducted. Preliminary results were published by Sloan et al. (2024) in abstract form, which showed lower rates of REP (6/22 patients, 27%) in this cohort. This is lower compared to historical controls from the mentioned meta-analysis by Waqar et al. (45.9%). Among these patients with REP, 5 patients have lesions adjacent to the cavity and 1 patient has lesions distant to the cavity. This reflects the diffuse and infiltrative nature of this tumor, and still the need for giving external beam radiation therapy to cover the microscopic disease. Interestingly in the subset of patients with subtotal resection or near-total resection, the residual tumor showed Rapid Early Response (RER) in 3/8 patients (38%). RER is defined as decrease in size of the residual disease, as seen from the postoperative MRI and the pre-chemoradiation MRI. With this promising data, final results and publication of the full manuscript are awaited by this year.

To determine a higher quality of evidence with the efficacy of GammaTile™ in addition to the current standard of care, BRIDGES (Beginning Radiation Immediately with GammaTile™ at GBM Excision vs Standard of care) trial was designed. This is a Phase 3 randomized clinical trial comparing standard of care alone (using Stupp protocol) vs standard of care with addition of GammaTile™ in the immediate adjuvant setting. The trial is currently ongoing activation, and will begin patient accrual this year (Agarwhal, 2026).

The use of GammaTile™ alone has also been explored. In this case series by Yekula et al., (2024), they prospectively followed 7 treatment-naïve GBM patients with rapid proliferation (defined as >100% tumor regrowth after surgery and prior to radiotherapy planning). In these patients, 3 of which are newly-diagnosed GBM, and 4 of which are recurrent IDH wild-type GBM. No surgical complications and 30-day mortalities observed, and only one 30-day readmission noted due to hydrocephalus requiring shunting. With a median follow-up 11.6 months, median overall survival was 10 months and 11.5 months for recurrent and newly-diagnosed GBM patients. Meanwhile, median overall progression-free survival was 10.6 months in both groups. This study shows that GammaTile™ alone can offer favorable local control and safety profile in GBM patients with rapidly proliferating disease.

There is currently no prospective evidence with the use of GammaTile™ for reirradiation of GBM in the recurrent setting. Given the conventional radiobiologic principles in previously-irradiated recurrent tumors, recurrent GBM tumors are inherently radioresistant. Giving the same or higher dose from the initial radiation therapy will concomitantly increase the risk of radionecrosis of the brain parenchyma. But giving a lower dose from the initial treatment will only have modest local control benefits at best. This dilemma poses a therapeutic challenge in this particular clinical scenario, yet it provides an opportunity for the use of GammaTile™. Brachytherapy in this setting may deliver high enough Biologically Effective Dose to the postoperative cavity, with steep dose fall-off that may potentially spare the previously-irradiated normal brain parenchyma. Gessler et al., (2021) reported a case series of 22 IDH wild-type GBM patients who underwent initial radiotherapy and concurrent/adjuvant temozolomide, and treated with maximal safe resection and GammaTile™ at the time of recurrence. Local control at

6 months and at 12 months were 86% and 81% respectively. Median overall survival was 20 months for MGMT-unmethylated, and 37.4 months for MGMT-methylated patients. Existing data with moderate quality of evidence led to the conditional recommendation with the use of brachytherapy for reirradiation in patients with recurrent GBM (Yeboa et al., 2025).

IX. Cost and Accessibility Considerations

Despite encouraging clinical outcomes, widespread adoption of GammaTile cesium-131 (Cs-131) brachytherapy in the Philippines may be limited by significant financial and infrastructural demands. GammaTile therapy requires specialized radioactive collagen implants, brachytherapy treatment planning systems, radiation safety infrastructure, and coordinated neurosurgical and radiation oncology services. Because Cs-131 sources are not locally manufactured, procurement and importation may substantially increase overall treatment costs and logistical complexity [1,35].

Although exact commercial pricing is not routinely disclosed in published literature, GammaTile implantation is generally more costly than conventional postoperative radiotherapy because of isotope acquisition, operating room integration, medical physics support, and postoperative imaging requirements. In the Philippine setting, the total procedural cost may reach several hundred thousand pesos per patient, potentially limiting accessibility to selected tertiary institutions [3].

Implementation of a GammaTile program also requires a multidisciplinary infrastructure involving neurosurgeons, radiation oncologists, medical physicists, neuroradiologists, radiation safety officers, and trained operating room personnel. Ferreira et al. emphasized that institutional implementation requires formal protocols for source commissioning, dosimetric verification, radiation surveys, and regulatory compliance. Specialized treatment planning systems capable of TG-43-based calculations, calibrated well chambers for source verification, and postoperative CT/MRI fusion capability are also necessary for safe clinical implementation [3].

Given these resource requirements, GammaTile therapy in the Philippines will likely remain limited to highly specialized neuro-oncology centers with established brachytherapy and medical physics support. Nevertheless, it may offer important clinical value in selected patients with recurrent or previously irradiated brain tumors.

X. Conclusion and Future Directions

GammaTile cesium-131 (Cs-131) brachytherapy is a promising intracranial radiation modality that enables immediate postoperative radiation delivery with favorable dosimetric and radiobiologic properties. Its steep dose falloff and rapid dose delivery make it particularly attractive for recurrent, previously irradiated, and high-risk brain tumors, with early studies demonstrating encouraging local control and acceptable toxicity profiles.

However, widespread implementation remains limited by high costs, isotope procurement challenges, and the need for specialized multidisciplinary infrastructure, particularly in resource-limited settings such as the Philippines.

Ongoing prospective studies are expected to further clarify long-term efficacy, safety, optimal patient selection, and comparative outcomes against established postoperative radiation techniques.

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