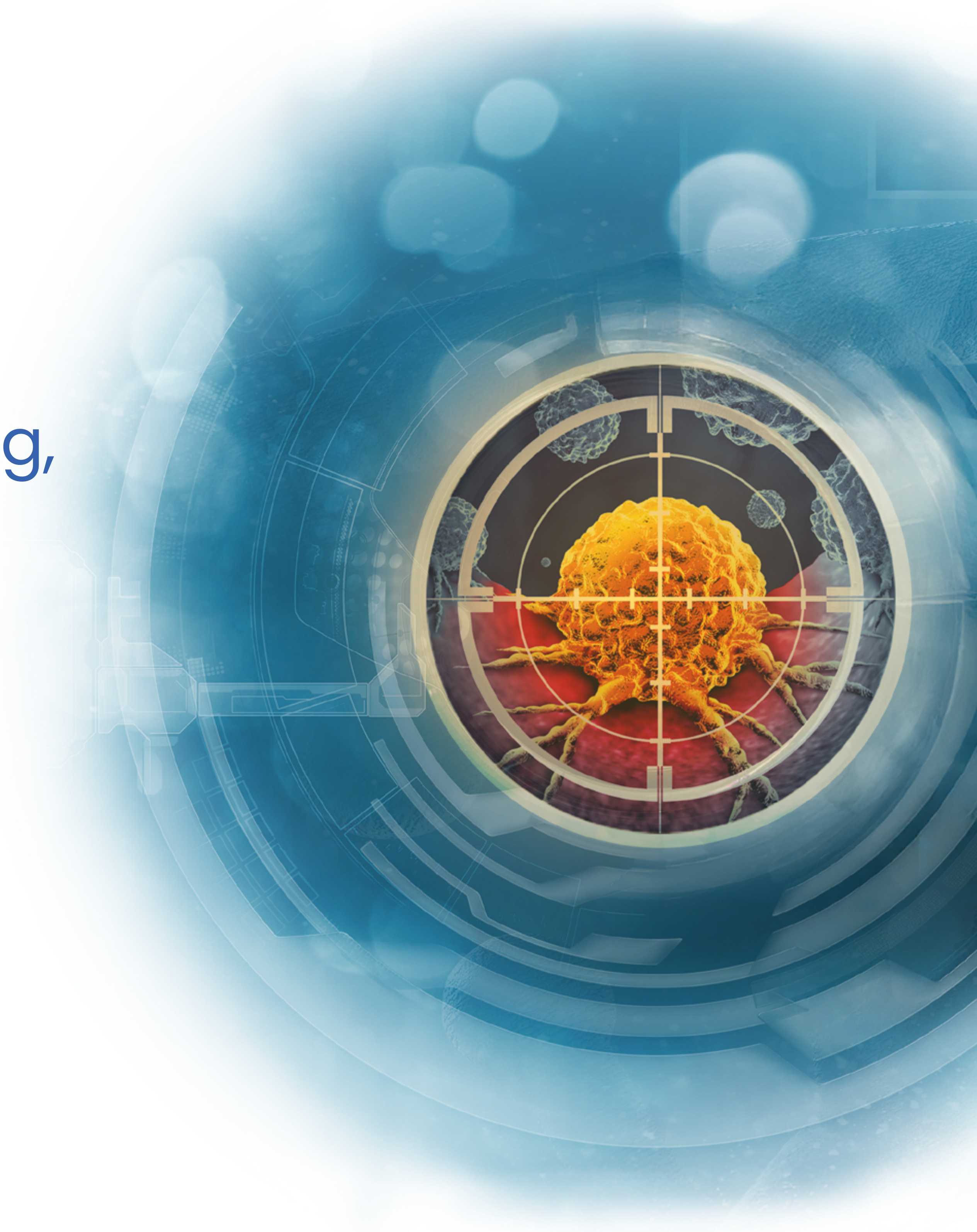
Impact Report 2025



Precision targeting, **global impact:**

cancer radiotherapy in the 21st century

Foreword

Radiotherapy has long been the unsung hero of cancer treatment. Nearly half of all cancer patients will need it, and it contributes to around 40% of cures. Yet despite this central role, radiotherapy remains underrepresented, underfunded, and misunderstood, marginalized in policy, planning, and investment. That imbalance drove me to advocacy. As a clinical oncologist, I have seen both the transformative power of radiotherapy and the devastating consequences when patients cannot access it in time.

It is a paradox of our time: while radiotherapy technology has advanced at breathtaking speed—highly precise treatments, adaptive techniques that personalize care, AI-driven planning—patient access has lagged. Too often, implementation falls behind discovery, with only large academic centers able to offer advanced care. This is not just a missed opportunity. It is a systemic failure we can correct.

Today, we stand at the edge of an enormous opportunity: to unleash the full potential of radiotherapy with the right investment, planning, and commitment to ensure access for every community around the world.

Global Disparities, Local Consequences

Nowhere is this need more urgent than in low- and middle-income countries, where access is minimal or non-existent. Entire populations are left without one of the most effective, scalable, and cost-efficient cancer treatments—treatment that could cure cervical cancer, control prostate cancer, or relieve pain. To deny radiotherapy is to deny care. Yet it does not need to be this way. Radiotherapy is not a luxury. It is a cornerstone of modern oncology and one of the soundest investments in healthcare. Every dollar invested delivers not only human benefit but also economic return, as patients return to work and communities thrive.

What Radiotherapy Needs Now: Leadership, Not Empty Words

What is required is leadership, vision, and commitment. Radiotherapy must be at the heart of every national cancer control plan, supported by:

- Modern equipment that is maintained and upgradable
- A trained workforce empowered to deliver innovation
- A global commitment to equitable access

We must also think globally, treating radiotherapy as one interconnected system. Machines delivered to sub-Saharan Africa or Eastern Europe cannot sit idle. They must anchor functioning ecosystems of training, mentorship, maintenance, and data to guide continuous improvement.

Adaptive radiotherapy represents a transformative leap—treatments tailored in real time, maximizing tumor control while sparing healthy tissue. We must seize this moment. Because if we are serious about curing cancer, reducing inequalities, and delivering value for patients, radiotherapy is not optional. It is indispensable.

Professor Pat Price

Clinical Oncologist, Founder and Chair of Radiotherapy UK, Visiting Professor Department of Surgery and Cancer, Imperial College London, Co-Founder and Chair of the Global Coalition for Radiotherapy

Table of Contents

Every minute approximately 38 people receive a cancer diagnosis, and 19 people die from this disease worldwide.*

Despite important advances in prevention and treatment, the global burden of cancer is expected to grow significantly over the next 25 years, with an estimated 35 million cancer diagnoses and 18.5 million cancer deaths in 2050.[2]

These estimates are today's projections, but we have the power to keep them from becoming tomorrow's reality.

Expanding access to radiotherapy could save 1 million lives each year.[3]

*Calculated based on 9,743,842 deaths and 19,976,499 diagnoses in 2022.[1]

Radiotherapy is a foundational and revolutionary part of cancer care

Since its initial use 125 years ago, radiotherapy (RT; also known as radiation therapy) has continuously evolved. It's a **foundational and revolutionary** part of modern medicine, more impactful than ever in 2025. It is estimated that more than half of cancer patients worldwide receive RT as part of their treatment regimen.[4]

The transformative power of technology innovation

Today's phones and cars are worlds away from the 19th century technologies on which they are based. The same is true for 21st century RT technology.

Just as current AI-enabled smart phones and self-driving cars seem worlds away from the 19th century technologies on which they are based, RT today is personalized, precision medicine that has eclipsed the wildest predictions of its early practitioners. In fact, patients receiving RT today benefit from transformative improvements in efficacy, safety, and clinical outcomes that weren't feasible even a decade ago.

Whether used as stand-alone therapy or in combination with surgery, chemotherapy, or biologic therapies, RT is an essential pillar of cancer care. Across multiple cancer types, recent advances in treatment planning and delivery technologies are making RT more impactful than ever before—providing more patients with precision therapy uniquely tailored to their tumors, prolonging more lives, and helping to cure more cancers.

Ongoing RT innovation will further improve treatment access and outcomes

Even as today's patients benefit from the historical advances that have made cutting-edge RT a precision medicine approach, ongoing innovation and the increased integration of AI holds the promise of providing bigger impact and better outcomes tomorrow.

In addition to enhanced safety and efficacy, advanced RT regimens require fewer treatment sessions. This means patients spend less time and money traveling to and from treatment centers, which can help reduce treatment-related stress and disruption to their daily routines. Regimens with fewer treatment sessions also increase care centers' treatment capacity, provide cost savings, and allow better allocation of RT resources and personnel. This helps make care more accessible.

Realizing the full potential of RT will take more than just 21st century technology. Increasing the availability of RT solutions and trained personnel is essential for meeting patients' needs as the global incidence of cancer continues to rise. Equally important is the implementation of access and reimbursement policies to guarantee that every patient who could benefit from RT receives it. Overcoming these challenges will demand new strategies from both government and industry leaders. Yet, each of us has the power to make a difference in the lives of cancer patients, whether they are close to us or in distant parts of the world. Our collective actions, large and small, will make the impact on cancer that all of us need.

"RT plays a central role in providing curative therapy to patients with head and neck cancer in most scenarios, sometimes in combination with surgery. There's a direct connection between head and neck cancer mortality and underinvestment in RT. This underscores the critical importance of increasing access to safe and effective RT around the world."

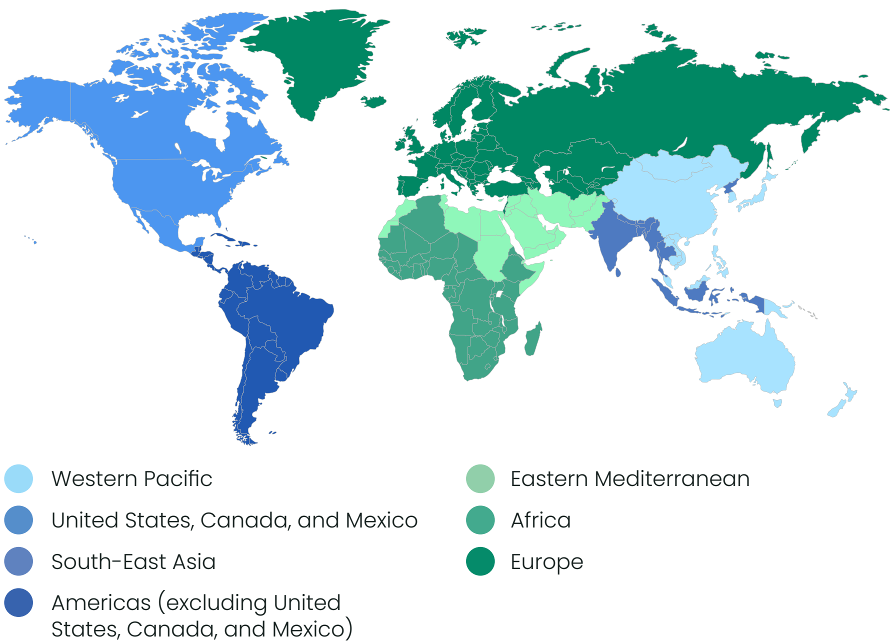
— Dr. Anthony Paravati, Executive Medical Director of Cancer Care and Chief of Radiation Oncology at Kettering Health

Cancer is a growing global health threat

Cancer is the second leading cause of death globally.[5]

Every minute approximately 38 people receive a cancer diagnosis, and 19 people die from this disease worldwide.* By the time you finish reading this report, cancer will impact hundreds of more lives. With an estimated one in six people developing cancer in their lifetime[5], most of us know someone who is living with cancer, is a cancer survivor, or has lost their battle against a disease expected to cause 10 million deaths this year.[6]

Despite important advances in prevention and treatment, the global burden of cancer is expected to grow significantly over the next 25 years, with an estimated 35 million cancer diagnoses and 18.5 million cancer deaths in 2050.[3] Today, the estimated growth of cancer's burden over the next 25 years is a projection; it's incumbent on all of us to ensure that it doesn't become a reality. Continued innovation in cancer prevention, early diagnosis, and treatment is essential for saving millions of lives that will otherwise be lost.



*Calculated based on 9,743,842 deaths and 19,976,499 diagnoses in 2022.[1]

Global incidence and mortality of cancer[1]

Region	Incidence	Mortality	Mortality/ Incidence
Western Pacific	6,818,489	3,475,128	51%
Europe	4,878,513	2,211,362	45%
United States, Canada, and Mexico	2,879,441	802,436	28%
South-East Asia	2,369,106	1,527,959	64%
Americas (excluding United States, Canada, and Mexico)	1,340,425	651,150	49%
Africa	901,201	586,046	65%
East Mediterranean	781,574	485,347	62%

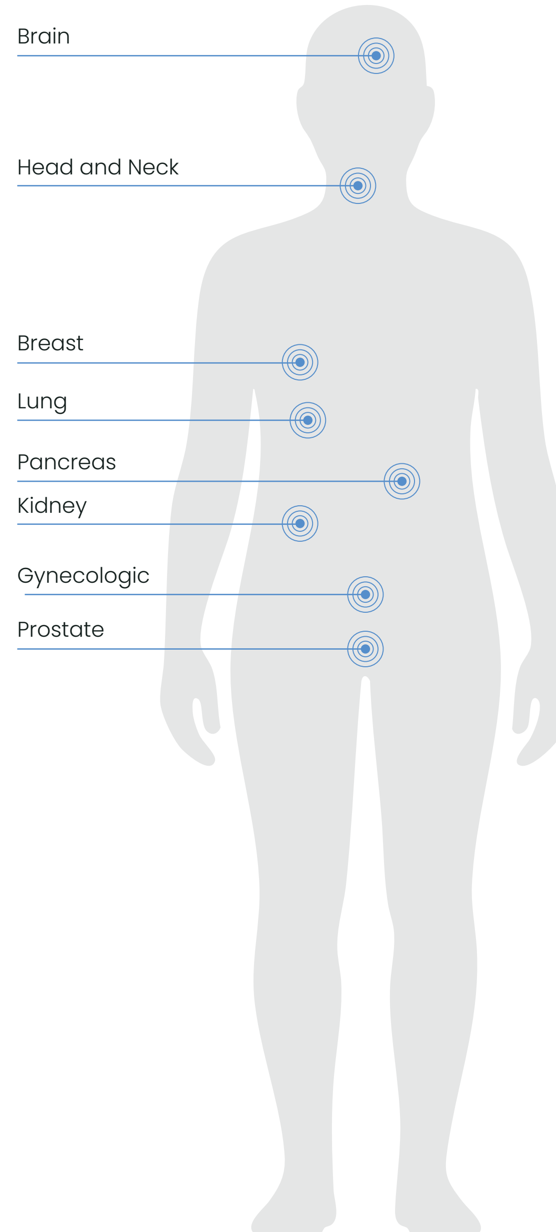
Multiple diseases with a common cause

While cancer can occur in different tissues and cells throughout the body, all cancers share a common cause: uncontrolled cell growth and division due to mutations within the cell's DNA.[5]

These mutations may be inherited, occur due to errors in DNA replication during normal cell division, or result from exposure to environmental factors.[5] Cancers that occur in organs or tissues typically form masses known as solid tumors, while cancerous blood or immune cells circulate throughout the body.[5] Solid tumors can also spread to other parts of the body, a process known as metastasis.[5]

Incidence and mortality of select cancers[1]

Cancer Type	Incidence	Mortality
Lung	2,480,675	1,817,469
Breast	2,296,840	666,103
Gynecologic (Includes uterus, cervix, ovaries, vagina, vulva)	1,473,427	680,372
Prostate	1,467,854	397,430
Head and Neck (Includes lip, salivary glands, oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx)	947,211	482,428
Pancreas	510,992	467,409
Renal (kidney)	434,840	155,953
Brain	321,731	248,500



RT is — and will continue to be — a cornerstone of cancer care

RT is a highly localized treatment that is effective against many types of cancers and is generally well tolerated, which is one of the reasons that more than half of cancer patients worldwide receive it at some point during their treatment journey.[4]

RT harnesses the energy carried in high-energy electromagnetic waves or particles to damage DNA, leading to cell death. While cells that are actively dividing, such as cancer cells, are more susceptible to this type of damage, healthy cells may also be affected.[7] This is why the ability to precisely deliver radiation to the tumor while sparing surrounding tissues and organs is critical for balancing the efficacy and safety of RT and optimizing patient outcomes.[7]

RT can be used as standalone therapy or combined with other treatments. It can be used prior to surgery to reduce the size of the tumor (neoadjuvant therapy), or after surgery to remove any cancer cells that may be left behind (adjuvant therapy).[8] Chemoradiotherapy, which combines RT with chemotherapy, is frequently used to treat locally advanced cancers and may provide enhanced efficacy by attacking cancer cells through two different mechanisms of action.[9] In some cases, such as prostate cancer, External Beam Radiation Therapy (EBRT) may be used in combination with brachytherapy to "boost" the dose of radiation delivered to the tumor.[10] Recent studies also support the potential for RT in combination with immunotherapies to provide enhanced tumor cell killing and prevent recurrence.[11]

Radiation kills cells by damaging DNA

Because healthy cells typically recover from radiation exposure more quickly than tumor cells, conventional RT regimens deliver the desired radiation dose over multiple treatment sessions, known as fractions.[7] This approach helps to destroy the maximum number of tumor cells possible while minimizing damage to healthy tissues and organs near the tumor. For example, conventional RT for prostate cancer is typically administered in 35-45 fractions, with one fraction given during each treatment session and treatment lasting 6-8 weeks.[12]

Newer RT technologies enable much more precise targeting of radiation directly to the tumor. This allows the radiation dose to be delivered in fewer fractions (known as hypofractionation) without increasing the risk of damage to nearby tissue. For example, Stereotactic Body Radiation Therapy (SBRT), an advanced RT technique, allows prostate cancer to be treated in only four or five fractions,[12] reducing patients' treatment burden and improving their quality of life during treatment.

In addition to directly killing cancer cells via DNA damage mechanisms, RT also can alter immune responses within the tumor microenvironment.[13] This triggers an anti-tumor response and also suppresses mechanisms that cancer cells use to escape immune system detection and clearance.[13] Some advanced forms of RT (Stereotactic Radiosurgery [SRS], Stereotactic RT [SRT] and SBRT) also destroy the blood vessels that provide the tumor with nutrients, indirectly leading to tumor cell death.[14]

“Technology innovation has been a key driver of recent RT advances. Incorporating cancer biology into patient selection and treatment planning will provide the next leap forward in personalizing RT. Initial work with Personalized Ultra-fractionated Stereotactic Adaptive Radiotherapy (PULSAR) suggests that very high doses of radiation delivered at much longer intervals (weeks or months) than current regimens may improve outcomes by leveraging radiation-induced changes in the tumor microenvironment for safer and more effective destruction of cancer cells.”

— Dr. Robert Timmerman, Chair of the Department of Radiation Oncology, UT Southwestern Medical Center

Multiple RT delivery methods enable personalized treatment regimens

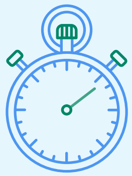
RT can be delivered using radiation sources located outside the body (EBRT) or placed inside the body (brachytherapy or systemic therapy).[8]

EBRT is most commonly administered using a machine known as a linear accelerator (linac). This machine accelerates electrons to high speeds and targets them to a tungsten plate. The collision of the electrons and the plate creates a beam of high-energy x-rays that is directed to the tumor, and the beam is shaped to maximize tumor targeting while minimizing exposure to healthy tissue.[15] The linac rotates around the patient, who lays on the treatment couch, allowing tumor targeting from multiple directions.[15] EBRT also can be administered using protons rather than high-energy x-rays (known as proton therapy).[16]

For internal radiation therapy, the radiation source is placed inside the body. Internal radiation therapy is called brachytherapy when the radiation source is a solid material, and systemic therapy when the radioactive material is in liquid form that is injected or swallowed.[8]

Common RT approaches

Intensity Modulated RT (IMRT) enables more precise targeting of radiation, with higher doses delivered to the tumor and reduced dosing to surrounding tissue.[17]



Volumetric Modulated Arc Therapy (VMAT) is an advanced form of IMRT that delivers radiation with a beam that moves in an arc around the patient rather than firing the beam multiple times from different directions. VMAT typically uses fewer beam firings in each treatment session than IMRT, reducing session time.[18]

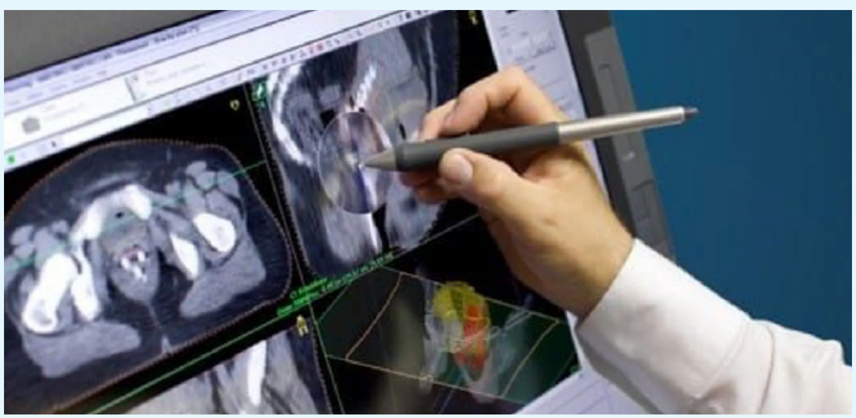
SRS uses multiple beams to target tumors in the brain in a single fraction.[19]

SBRT applies the principles of SRS to parts of the body other than the brain, with treatment typically delivered in 1-5 fractions.[20]

Proton therapy uses high-energy protons rather than high-energy x-rays to kill cancer cells.[21]

Systemic internal radiation therapy uses radioactive liquids that are swallowed or injected and travel through the body to tumor sites.[8]

Brachytherapy utilizes radioactive pellets, capsules, or ribbons that are placed in (interstitial brachytherapy) or near (intracavity brachytherapy) the tumor,[8] in as few as one or two fractions.



EBRT is the foundation for a variety of RT techniques

IMRT, VMAT, SRS, SBRT, and Stereotactic Ablative Body Radiotherapy (SABR) are advanced linac-based EBRT techniques that enable more precise delivery of radiation to the tumor while minimizing exposure to healthy tissue.[15]

This precision can allow the use of higher doses, which may improve efficacy, while minimizing side effects.

For some types of early-stage cancers and cancers that are in the early stages of spreading to multiple sites in the body (sometimes referred to as oligometastases), SBRT can provide locoregional control similar to surgery but without the side effects associated with surgical procedures.[24–28] This may allow patients who are contraindicated for surgery due to other health issues to receive highly effective therapy. Improved outcomes achievable with advanced RT techniques may delay or prevent the need for therapies with more side effects in patients with some types of oligometastatic disease, which can improve patients' quality of life.[27–29]

How can you precisely eliminate something that you can't see?

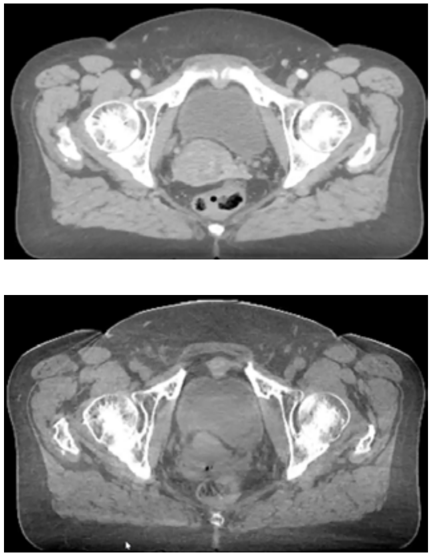
For decades, this was a critical challenge (and limitation) of RT. In the first 70 years of cancer RT, radiation dosing and targeting were determined using information from low-resolution x-ray images and physical exams.

This information was then correlated with externally visible anatomic structures (such as skeletal features) to position the beam during treatment. This approach made it difficult to target the tumor with precision and often resulted in exposing healthy tissue, which reduced efficacy and increased side effects.

The development of Computed Tomography (CT) imaging (also known as CAT scans) in the early 1970s made it feasible to determine RT dosing based on 3D representations of the tumor. CT scans use x-rays to capture multiple images, which are then combined to create higher-resolution, 3D models of the tumor. CT imaging also provides critical information about the position of the tumor relative to nearby organs and surrounding tissues, allowing the development of dosing regimens optimized for delivery to the tumor while minimizing exposure to healthy cells.

While CT provides very high-resolution images that can be used for RT treatment planning, it can't be used for repeat imaging during treatment because the high-energy x-rays used to create CT images would increase the patient's radiation exposure. The introduction of Cone-Beam CT (CBCT) imaging, which use lower-energy x-rays, allows 3D images to be captured during each treatment session without increasing the risk of imaging-related radiation. While CBCT images are lower resolution than those captured by CT, they still provide benefit by enabling in-treatment imaging that can be used to improve RT targeting and precision and enable hypofractionated regimens.

CT vs CBCT

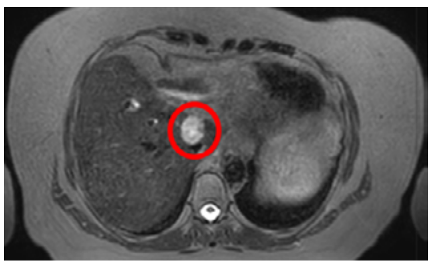


A CT image (top) provides greater detail and differentiation of tissue compared with a CBCT image (bottom).

MRI makes real-time, high-definition imaging during treatment a reality

The integration of Magnetic Resonance Imaging (MRI) into RT delivery systems in 2014 at last gave radiation oncologists the crystal-clear images they needed to see and differentiate the tumor from surrounding tissue in real time while radiation was being delivered.

MRI vs CT



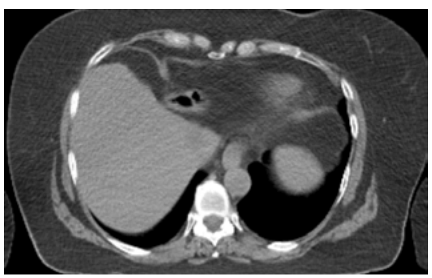


Photo courtesy of GenesisCare Sydney

MRI clearly identifies a liver tumor (circled in red in top image), while CT does not (bottom).

The use of algorithms that read and respond to real-time MRI data and shut off the radiation beam if the tumor moves out of the target area (known as real-time tracking and gating) provides unprecedented precision in RT. This is a critical advance because tumors and organs can move during the treatment session due to breathing, the movement of food and gas through the digestive system, bladder filling, and heart muscle contraction. It also occurs if patients move even slightly during treatment. The precision achieved with real-time tracking and gating also allows treatment to be completed in even fewer, higher-dose sessions (ultra-hypofractionation) and opens the door to treating tumors not amenable to conventional RT approaches.

ART in action

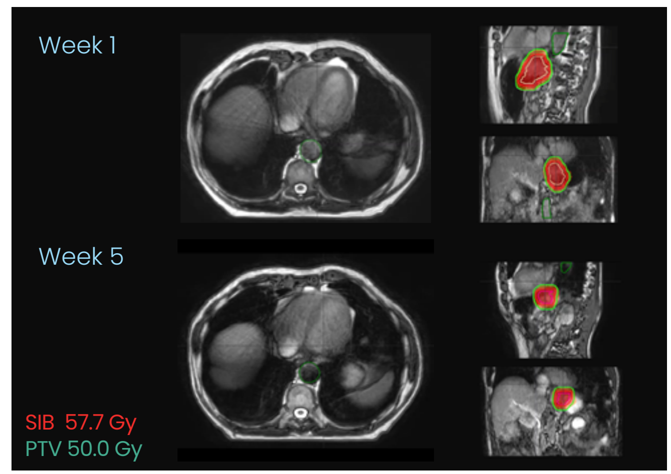


Photo courtesy of Başkent University

Click above to activate the MRI

Real-time MRI images captured during treatment of an esophageal tumor. The tumor (red) remains within the treatment target zone (green) throughout the treatment session. Adaptive replanning allows for a smaller target treatment area as the tumor shrinks over time (compare red and green between Week 1 and Week 5).

Adaptive RT

Precise and personalized treatment for every patient, every session.

CBCT and MRI technology combined with powerful algorithms and automation provide previously unimaginable solutions in the form of Adaptive RT (ART). Today, a treatment plan is a starting point that can be continuously adjusted every few sessions or even daily depending on the tumor's shape, size, and position relative to other organs. Head and neck tumors shrink and change shape slowly over time as they respond to therapy, but typically don't change position relative to surrounding tissues. Consequently, once- or twice-weekly adaptation is sufficient to maintain optimal dosing and targeting. In contrast, the position of tumors within the abdomen can change daily (and even during treatment) due to normal anatomical motion. This type of motion can be addressed with daily adaptation, ensuring optimal dosing based on the patient's anatomy at the time of treatment.

ART can be done using images taken while the patient is in or out of the treatment position (on-line or off-line ART, respectively).[30]

	Off-line ART	On-line ART
Timing	• Between treatment sessions	• Immediately prior to treatment
Patient Position	• Out of treatment position	• In treatment position
Use	• Tumors that change slowly over the treatment period	• Tumors that can change position between sessions • Positioning of brachytherapy applicators
Considerations	• Flexibility with respect to how and when images are captured	• Requires co-location of imaging and delivery devices in the same room or device • Requires rapid computing capabilities

ART has been shown to provide excellent efficacy with fewer side effects in multiple clinical studies

Trial	Key Findings
EBRT	
Prostate Cancer	
HERMES[31]	Patients can receive treatment in 2 sessions without increasing Grade 2 or greater (G2+) genitourinary (GU) side effects compared with 5 fractions.
ERECT[32]	Advanced RT imaging and delivery technologies can help preserve erectile function in men treated for prostate cancer.
MIRAGE[33]	MRI-guided reductions in margins can better protect organs and tissues around the prostate compared with CT-guided reductions, leading to significant reductions in G2+ GU and gastrointestinal side effects (GI) and improved patient-reported quality of life. 2-year follow-up data showed sustained benefit of MRI guidance with respect to G2+ GU and GI side effects, bowel function and sexual health.
Prostatectomy Adaptive Radiation Therapy (ART)[34]	ART can reduce dosing to the small bowel while effectively targeting the prostate in patients receiving RT after prostatectomy.
Brain Cancer	
UNITED[35]	Smaller margins can preserve more healthy brain tissue without increasing the risk of recurrence compared with larger margins for patients with high-grade gliomas.

Trial	Key Findings
Pancreatic Cancer	
SMART[36]	ART improved overall survival time and rates of 2-year survival, 2-year local control, and 2-year disease-free progression compared with results typically achieved with non-adaptive RT in patients with borderline resectable or locally advanced pancreatic cancer.
Head and Neck Cancer	
ART for Head and Neck Cancer[37]	Automated CBCT tracking that identifies anatomic changes can guide ART, potentially sparing salivary structures.
Daily ART for Head and Neck Cancer[38]	Daily CBCT-ART with reduced margins reduces exposure to some but not all organs at risk and significantly reduces rates of mucositis (but not other side effects), compared with non-adapted, image-guided RT.
Brachytherapy	
Cervical Cancer	
EMBRACE I[39]	Chemoradiotherapy with MRI-based image-guided adaptive brachytherapy (IGABT) provides long-term control of cervical cancer with low rates of long-term side effects.
EMBRACE II[40]	Treatment with IGRT-IMRT, cisplatin chemotherapy, and IGABT further improved survival and reduced side effects, making this regimen the standard of care for locally advanced cervical cancer.

RT in clinical practice

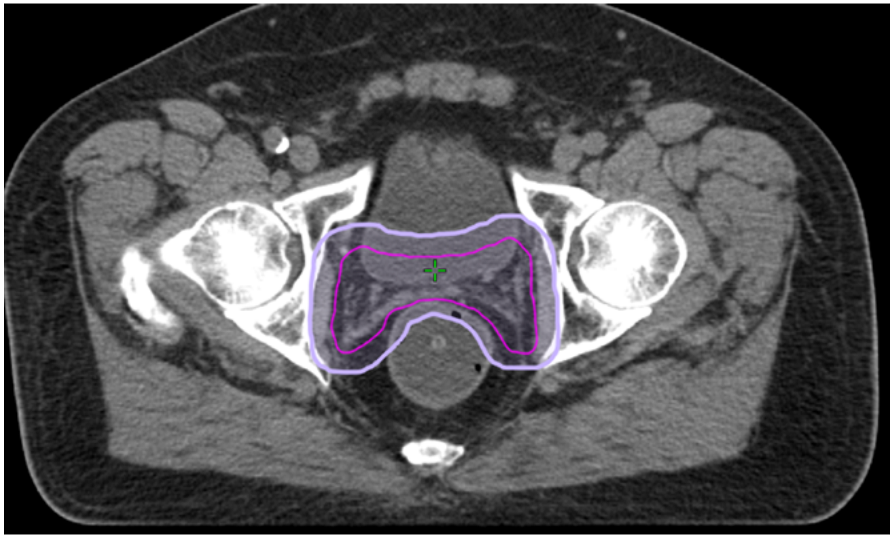
A key reason that RT is given to more than half of all cancer patients is its versatility as a standalone therapy or in combination with other treatment modalities and its utility at different stages of disease.

It can be used prior to surgery to reduce the size of the tumor (neoadjuvant therapy), or after surgery to remove any cancer cells that may be left behind (adjuvant therapy).[8] Chemoradiotherapy, which combines RT with chemotherapy, is frequently used to treat locally advanced cancers and may provide enhanced efficacy by attacking cancer cells through two different mechanisms of action.[41] In some cases, such as prostate cancer, EBRT may be used in combination with brachytherapy to "boost" the dose of radiation delivered to the tumor.[42] Recent studies also support the potential for RT in combination with immunotherapies to provide enhanced tumor cell killing and prevent recurrence.[43]

Radiation doses are measured in a unit called a Gray (Gy), and are determined based on the type of cancer, proximity of the tumor to critical organs, and the patient's overall health and ability to tolerate treatment. Treatments are planned with the goal of eradicating all cancer cells while protecting healthy tissue around the tumor. The Planning Tumor Volume (PTV) for radiation delivery typically includes the Gross Tumor Volume (GTV, defined by imaging studies), a margin around the GTV that includes tumor cells that may not appear on imaging (Clinical Tumor Volume [CTV]), and an additional margin around the CTV intended to account for potential variations in radiation delivery during treatment.[44]

In addition to defining the target dosing area, treatment plans also determine the total dose that will be delivered over the course of therapy and how to fractionate the dose to achieve the optimum balance between safety and efficacy.

PTV reductions spare more healthy tissue



This CTV (dark purple) is 132 cm^3 and the PTV (light purple) is 348 cm^3, which includes 216 cm^3 of normal tissue. Dosing these 216 cm^3 does nothing to fight cancer and is the cause of side effects. Even small changes in PTV can have significant effects on the volume of normal tissue exposed to radiation.

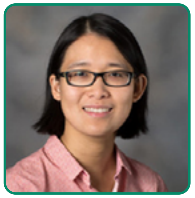
RT is team medicine

While team composition may vary among locations and countries, members may include[45]:

- **Radiation oncologist –** a physician who has completed specialized training using RT to treat cancer. The radiation oncologist oversees each patient's care, develops the treatment plan, ensures each fraction is delivered correctly, adapts treatment as needed, and monitors the patient's progress. The radiation oncologist also collaborates with surgeons and medical oncologists when patients are receiving combination therapy.
- **Medical physicist –** works with the radiation oncologist on treatment planning and is also responsible for ensuring the quality and safety of RT equipment.
- **Radiation therapist –** plays a critical role in both treating and supporting patients by working with the RT team and pairing RT knowledge with expert understanding of technology.
- **Dosimetrist –** works with the radiation oncologist using treatment planning software to develop the detailed map of radiation dosing that optimizes tumor targeting while protecting as much healthy tissue as possible.
- **Radiation oncology nurse –** works with the RT team to support the patient throughout the treatment journey. Radiation oncology nurses help evaluate patients prior to the initiation of treatment and are often the first point of contact for addressing problems and concerns the patient may have during treatment.

Because RT can be used in combination with surgery and/or systemic therapy, the care team in many cases may also include surgical and medical oncology staff. Working together, interdisciplinary teams help patients understand their treatment options and design regimens tailored to each patient's cancer.

"The multi-disciplinary aspect of radiation oncology really appealed to me and is a key reason I entered the field. Providing excellent RT care requires close collaboration with the larger RT team, my surgical and medical oncology colleagues, and social workers, speech therapists, and nutritionists. Together, we ensure that patients are fully supported throughout and after their treatment journey."



— A/Prof. Sweet Ping Ng,
Consultant Radiation Oncologist, Austin Health, Melbourne Australia

Patient stories

Cheryl

It began as a tiny spot during a cold Louisiana winter, something that looked like nothing more than dry skin.

At the same time, Cheryl Michelet was experiencing severe arm pain and losing mobility. Physical therapy didn't help, so her doctor referred her to an orthopedist, then to a surgeon who suspected a rotator cuff tear and ordered an MRI. Cheryl had never missed a mammogram, but it was this MRI—taken for her shoulder—that revealed what her screenings had not.

Cheryl recalls the shift in her doctor's tone as he explained that an enlarged lymph node had been found and that she needed to go to Women's Hospital right away.

A breast specialist confirmed the concern. About 1–5% of breast cancers do not appear on mammograms or ultrasounds, only on MRI or PET scans. Within days, a biopsy confirmed stage III breast cancer.

Her care team moved quickly, what Cheryl described as the "speed of light" to start "monster chemo," a demanding course of multiple rounds of chemotherapy. In November 2020, she underwent a mastectomy. A follow-up PET scan showed no signs of cancer.

Cheryl then faced a critical decision. Although her scans were clear, lymph node removal was recommended to assess disease extent. Even after surgery, microscopic cancer cells could remain posing a risk of recurrence.

Radiation therapy was a critical next step, targeting high-risk areas beyond what surgery could address to eradicate residual disease and improve long-term outcomes. Cheryl proceeded with daily radiotherapy for six weeks alongside chemotherapy every three weeks, grateful for the support and skill of her care team. "I had trust in the people around me and once we got started it was just a routine. Of every part of the process, I would say [radiation therapy] was the easiest."

Now, Cheryl looks ahead with hope and purpose—celebrating milestones with her family while using her experience to support and advocate for other patients on their journeys.

> "I had trust in the people around me and once we got started it was just a routine. Of every part of the process, I would say [radiation therapy] was the easiest."
>
> — *Cheryl Michelet*

Mark

Leading an active life comes with its share of sports injuries, as Mark Meyer knows well. He dealt with these with his usual resourcefulness.

But when he noticed blood in his urine, he realized he needed to seek medical attention.

In the summer of 2021, Mark was diagnosed with FH-deficient renal cell carcinoma, a rare kidney cancer, and when two very complicated metastasis arose in January 2025, a long and challenging journey to access treatment began.

A physician made Mark aware of a new technology called the MR-linac, a type of medical linear accelerator offered at select treatment centers. Navigating public insurance across multiple unaffiliated centers, he faced numerous barriers. "There's no one to talk to. There is no managed care at all," he said. "The patient literally has to do everything." Determined to access it, Mark researched centers that offered the MR-Linac for his treatment and ultimately found that the University of Iowa Holden Comprehensive Cancer Center provided adaptive radiation therapy, which uses advanced MRI technology to tailor treatment to each patient's tumor.

The MR-linac was recommended for Mark because it provides real-time imaging, allowing radiation to be precisely targeted to the tumor while protecting healthy tissue and reducing side effects.

Unlike traditional radiotherapy, which often requires 30 or more treatment sessions, his treatment was completed in just five sessions. By the time he finished his final treatment on July 18, Mark showed no signs of cancer spread.

Despite fatigue during treatment, he remained active, enjoying golf and tennis with his sister. Though he admits with cancer metastasis, "the reality you wake up to is worse than your nightmares," he has regained his strength post-treatment and feels more like himself today.

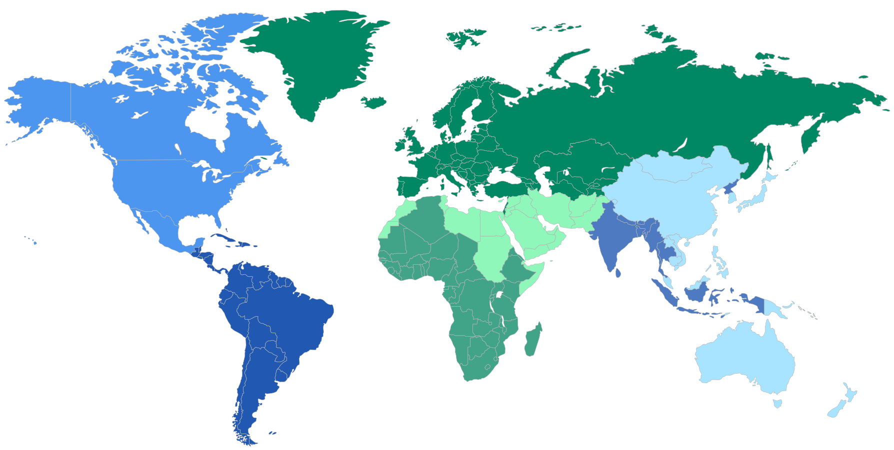
Once a "sports guy on the business side," Mark now helps others navigate cancer and travels with a renewed perspective, hoping to inspire joy even in dark times. "Like the Tom Petty song, the waiting is the hardest part," he remarked.

RT in prostate cancer

Globally, prostate cancer is the second-most diagnosed cancer in men, and it's the most commonly diagnosed cancer in men in 118 of 185 countries.[46]

Prostate cancer may be treated in several ways, including removal of the prostate (prostatectomy), radiotherapy, hormone therapy, chemotherapy, and targeted therapy.[47] Radiotherapy is a mainstay of prostate cancer treatment and can be used in all stages of disease.[47] For some patients, radiotherapy (low-dose brachytherapy, high-dose brachytherapy, IMRT, SBRT, or ART) may be the only treatment needed to cure their cancer, while others may receive radiotherapy in combination with other modalities to cure or control disease or to relieve disease symptoms.

Because it plays a critical role in male urinary and sexual functions, cancer therapy that removes or damages the prostate can lead to urinary incontinence and impotence. This can reduce patients' quality of life post-treatment even if their cancer is cured. Consequently, improving the precision of tumor targeting and minimizing damage to healthy prostate tissue and nearby organs (including the bladder and rectum) is critical for maintaining patient quality of life.



Global incidence and mortality of prostate cancer[1]

Region	Incidence	Mortality	Mortality/ Incidence
Europe	498,433	123,645	25%
Western Pacific	298,759	78,021	26%
United States, Canada, and Mexico	282,250	46,951	17%
Americas (excluding United States, Canada, and Mexico)	198,751	53,434	27%
Africa	89,171	49,656	56%
South-East Asia	64,009	29,520	46%
East Mediterranean	35,287	15,760	45%

Advances in imaging and radiation delivery technologies—including ART approaches—are enabling unprecedented precision in radiotherapy. This improves efficacy, reduces side effects, and also supports ultra-hypofractionated regimens that can be delivered in as few as five sessions for patients with prostate cancer.[48] Promising clinical data also suggest that treatment can be delivered in two sessions without increasing side effects.[31]

Benefits of ART in prostate cancer

- Potential for treatment with 2 fractions rather than 5 fractions without increasing Grade 2 or higher (G2+) genitourinary (GU) side effects.[31]
- Reduced risk of post-treatment erectile dysfunction compared with conventional RT.[32]
- Use of smaller margins enabled with MRI guidance better protects nearby organs and reduces G2+ GU and G2+ gastrointestinal side effects for up to 2 years compared with CT guidance.[33]
- Daily replanning ensures that desired tumor dosing and organ sparing is achieved with every fraction.[34]

Dr. Himanshu Nagar, MD, MS, Director, Genitourinary Program, Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center

"The prostate gland is very close to the bladder, rectum, and bowel. X-ray images don't provide sufficient contrast to differentiate the tumor from surrounding healthy prostate tissue or to determine the precise location of the tumor relative to these organs. Many men now live for decades following treatment for prostate cancer, so there's a growing need to balance near-term eradication of the tumor with long-term sexual, urinary, and bowel function. Advanced imaging technologies that better visualize the tumor now allow us to maximize tumor dosing while protecting nearby organs with unprecedented precision. This precision is the foundation for ultra-hypofractionated regimens that allow patients to be treated in five or fewer sessions, reducing disruptions to their work and daily activities and minimizing travel costs. This reduction in burden may make RT more accessible to patients who prefer a noninvasive treatment option but prefer not to undergo 4-8 weeks of conventional RT treatment.

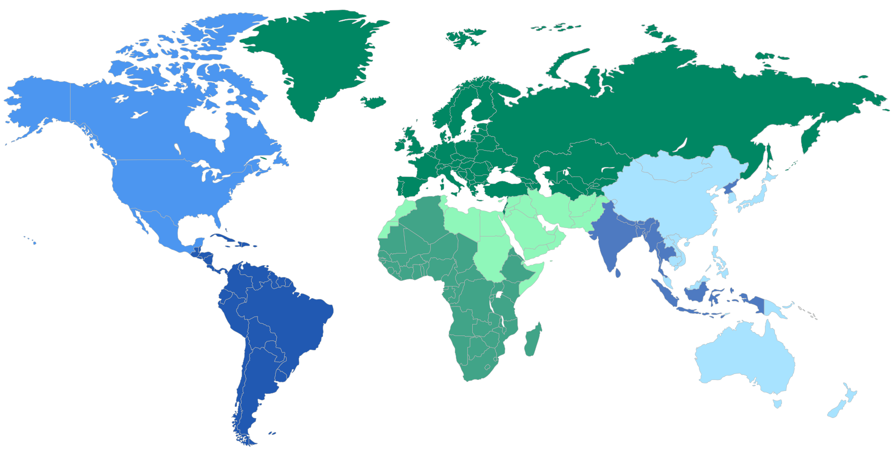
Today, ART with real-time imaging enables tailored, personalized prostate cancer treatment. Each daily plan is adapted based on the tumor's size, shape, and location relative to other anatomy at the moment of treatment. With real-time motion tracking and gating technology, we track therapy during treatment, ensuring that the beam is on only when the tumor is within the target area and critical organs are out of it. This wasn't an option when I began my career ten years ago, and I believe continued innovation will drive additional improvements in safety and efficacy of RT in a variety of cancer types."

RT in brain cancer

Median survival of glioblastoma is approximately 12-15 months.[49]

There are more than 150 types of brain tumors.[50] Gliomas account for 78% of malignant brain tumors that begin in the brain (primary brain tumors).[50] Tumors in the brain also can be due to metastasis of cancers that start in other parts of the body.[50] More than two-thirds of adults diagnosed with glioblastoma die within two years of diagnosis and it is also the most deadly solid tumor in children.[51] The global incidence of brain cancer is increasing.[52]

Surgery, RT, and chemotherapy are used to treat primary brain cancer and RT may be done with IMRT, VMAT, or proton therapy.[50] Traditional image-guided RT approaches for glioblastoma deliver radiation to large areas of the brain for 3-6 weeks, which can negatively affect cognitive function.[53] SRS can reduce cognitive decline compared with whole brain radiation in brain metastases[54] but is not used for glioblastoma due to the larger size of these tumors and need for larger margins to ensure tumor control. MRI-guided ART is enabling margin and dose reduction in the treatment of glioblastoma and recently has been proven to be safe and effective in patients with high grade gliomas (HGG).[35]



Western Pacific
United States, Canada, and Mexico
South-East Asia
Americas (excluding United States, Canada, and Mexico)
Eastern Mediterranean
Africa
Europe

Global incidence and mortality of brain cancer[1]

Region	Incidence	Mortality	Mortality/ Incidence
Western Pacific	104,875	69,710	66%
Europe	79,364	64,264	81%
South-East Asia	45,260	39,102	86%
United States, Canada, and Mexico	31,650	23,985	76%
East Mediterranean	25,024	21,545	86%
Americas (excluding United States, Canada, and Mexico)	23,418	19,821	85%
Africa	12,033	9,976	83%

Advanced RT in brain cancer

- OS and PFS using on-line weekly-adapted MR-guided ART with a smaller CTV in combination with chemotherapy was non-inferior to those historically achieved with larger margins.[35]
- New paradigm in the treatment of glioblastoma as the volume of normal brain tissue irradiated has been de-escalated.[35]
- SRS continues to advance the care of patients with brain metastases such that the number of brain metastases is less important than the technical ability to deliver treatment safely.[55]

Dr. Arjun Sahgal, Chief of Radiation Oncology, Sunnybrook Odette Cancer Center and President of the International Stereotactic Radiosurgery Society (ISRS)

"Early in my training I had limited exposure to using SRS for treating brain metastases. Most patients were treated with whole-brain RT, which was associated with effects like hair loss, fatigue, and memory loss in the short-term and dementia in the long term. When I moved to a center that was using SRS more routinely, it was really eye-opening. Seeing how well patients responded to SRS—even patients with multiple metastases—really made me a champion of the technology to help patients.

It's been exciting to see how new technologies and an evolving understanding of brain cancer biology are allowing us to make RT more effective and tolerable than ever before. Recently I treated a patient who had 80 brain metastases with SRS and we were able to complete the treatment in just seven days.

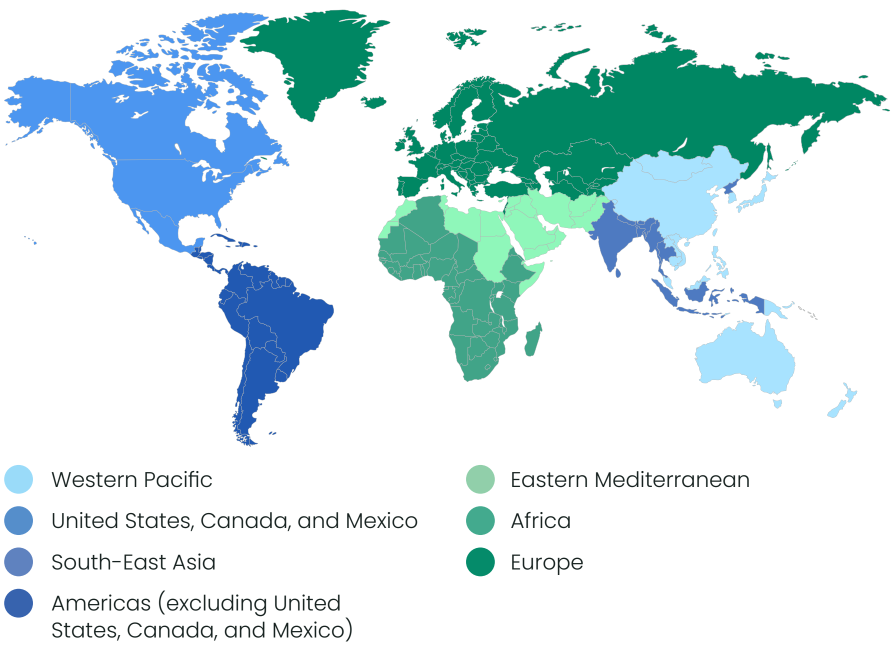
For glioblastoma, I had been waiting for a technology that would allow me to design a new paradigm and apply the principles of SRS but with a different bent. I wanted to reduce exposure of healthy brain tissue while still controlling disease effectively by de-escalating the volume irradiated and treatment adaption. MRI-guided linac technology has made weekly ART a reality, allowing us to reduce the margin to just 0.5 cm while still tailoring treatment to high-risk regions. This technology is critical to de-escalation, as we observed that HGG are not static. Adapting RT to changes in tumor volume and growth is essential for ensuring accurate dosing to the tumor and protection of healthy brain tissue. Sunnybrook Odette Cancer Center conducted the Phase 2 UNITED trial, the first trial designed to de-escalate standard 3- or 6-week RT with MRI-guided adaptive MR-linac therapy. UNITED demonstrated very promising safety and efficacy, and we are moving forward with additional trials that will inform how to use this novel approach to achieve even better outcomes for patients."

RT in lung cancer

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death globally in men; it's the second most common type of cancer and cause of cancer death in women.[1]

Treatments for lung cancer may include surgery, RT, chemotherapy, immunotherapy, and targeted therapy, and several of these modalities may be used in combination.[56] The choice of therapy is determined by lung cancer type (small cell or non-small cell), stage, molecular profiling, location within the lung, and the patient's overall health.[56]

RT is often used as curative treatment in patients with early-stage lung cancer who are not candidates for surgery, and may be used (often in combination with chemotherapy) to shrink a tumor before surgery or to kill any cancer cells that remain after surgery.[57] A recent study showed that treatment of non-small cell lung cancer (NSCLC) with SABR provided 10-year overall survival rates comparable to surgery.[58] Definitive RT with chemotherapy is the standard of care for medically inoperable, locally advanced NSCLC. RT is used as a consolidative therapy after systemic therapy in patients



Global incidence and mortality of lung cancer[1]

Region	Incidence	Mortality	Mortality/ Incidence
Western Pacific	1,306,393	905,728	69%
Europe	542,534	427,939	79%
United States, Canada, and Mexico	265,447	158,431	60%
South-East Asia	185,636	166,290	90%
Americas (excluding United States, Canada, and Mexico)	96,695	82,742	86%
East Mediterranean	54,708	49,384	90%
Africa	28,285	26,086	92%

with oligo-metastasis/progressive NSCLC. It can also be used for alleviating symptoms in patients with advanced lung cancer.[57] EBRT, proton therapy, and brachytherapy may be used at different stages of disease.[57]

The evolving role of RT in lung cancer

- Increased use of SBRT in early-stage NSCLC, especially for patients who aren't candidates for surgery, has significantly reduced the number of patients who received no treatment and improved overall survival.[59]
- SBRT can provide 10-year outcomes comparable to surgery in early-stage NSCLC.[58]
- RT is included in the first clinical guideline for the treatment of oligometastatic/progressive NSCLC.[60]
- SBRT is also used to treat pulmonary metastases that arise from other types of cancer, including breast, kidney, colorectal, prostate, sarcoma, and head and neck cancer.[61]

Dr. Joe Y. Chang, Director of the Stereotactic Ablative Radiotherapy Program at MD Anderson Cancer Center

"The precision we can achieve with today's RT technology is changing how we treat lung cancer. When I first began practicing, most of the patients I treated had stage III lung cancer. This was because earlier-stage disease was treated with surgery, and later-stage disease was treated systemically. Today, I'm treating more stage I and stage IV disease because advanced technologies allow us to target ablative radiation doses to the tumor in patients with stage I-II disease and to oligometastases in stage IV disease. We have shown that SABR can provide 10-year survival outcomes that are comparable to surgery for patients with early-stage lung cancer. SABR can also be used to control oligometastatic/progressive disease. One of my patients has had 24 oligometastatic/progressive lesions treated over the past 11 years. This wasn't considered possible when I began practicing.

ART using on-board MRI that enables real-time imaging is another important advance that can improve precision by addressing the motion that occurs as the patient breathes. With ongoing innovation in imaging technology, this may also be feasible with CBCT imaging in the future. New AI technologies also hold promise for making the replanning and adaptation process faster and even more precise."

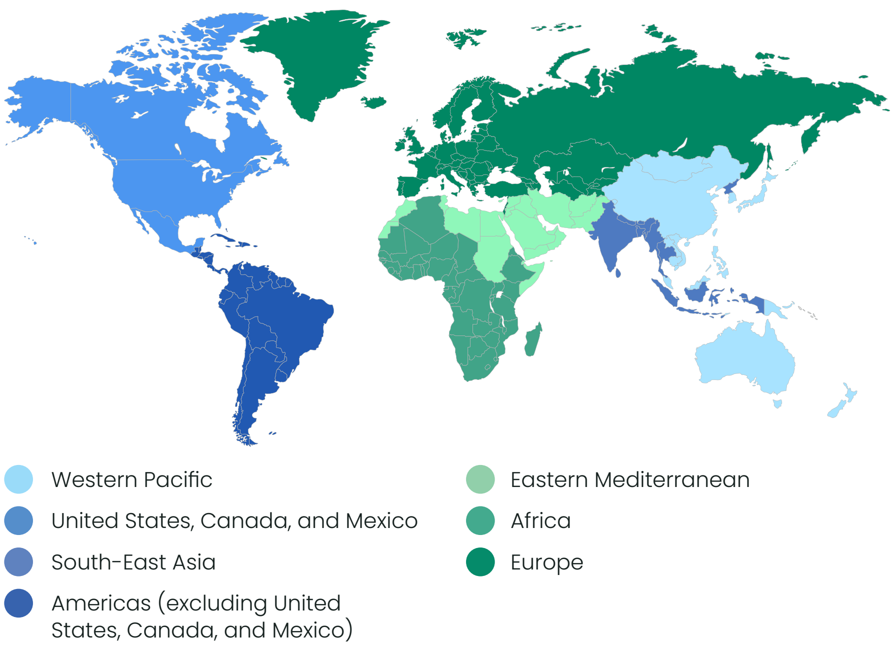
RT in renal cancer

The global incidence of renal cancer is expected to increase over the next decade.[62]

Renal (kidney) cancer can be treated surgically by removal of the entire kidney (radical nephrectomy) or the portion of the kidney where the tumor is located (partial nephrectomy), RT, other ablative therapy, or a combination of these treatments.[63] Disease that has spread outside the kidney typically is treated with systemic therapy (targeted therapy and/or immunotherapy).[63]

For many years, renal cancer was believed to be resistant to RT. However, a growing number of clinical studies have demonstrated that SBRT with radiation doses high enough to ablate the tumor (known as stereotactic ablative RT, or SABR) can be safe and effective across all stages of renal cancer.[64] In 2024, the International Society of Stereotactic Radiosurgery (ISRS) issued a practice guideline supporting the use of SBRT in primary renal cell carcinoma (RCC), the most common form of kidney cancer.[65]

While surgery typically is the primary therapy for stage I-III renal cancer, RT now is an important alternative for patients who aren't candidates for surgery due to other health conditions or prefer a non-invasive treatment option.[63] SABR also can be used to treat recurrence in the kidney or to treat oligometastatic or oligoprogressive disease outside the kidney.[27,28,63,64,66,67]



Global incidence and mortality of renal cancer[1]

Region	Incidence	Mortality	Mortality/ Incidence
Europe	155,178	55,950	36%
Western Pacific	112,114	37,473	33%
United States, Canada, and Mexico	86,169	20,351	24%
Americas (excluding United States, Canada, and Mexico)	29,456	12,281	42%
South-East Asia	25,827	15,403	60%
East Mediterranean	13,252	6,551	49%
Africa	12,747	7,906	62%

A recent study also found that RT with MRI-guided SBRT was a feasible, non-invasive treatment option for patients with localized RCC, and that this approach had minimal impact on kidney function.[68]

SBRT/SABR in renal cancer

Primary RCC

- 96.1% and 91.4% cancer-specific survival (CSS) at 2 and 4 years, respectively, with no grade 3-5 side effects.[69]
- 100% local control at median follow-up of 17 months and no grade 3-5 side effects with MR-guided adaptive SBRT.[68]

Oligometastatic RCC

- 100% 1-year overall survival and 82% 1-year systemic therapy-free survival (STFS) probability.[27]
- Overall survival was 94% and 87% at 2 and 3 years, respectively; 34-month median STFS.[28]

Oligoprogressive RCC

- SBRT delayed need to change systemic therapy for > 1 year.[66]
- 100% local control rate; > 6 month extended duration of ongoing systemic therapy; 11 months from SABR to new systemic therapy; 24-month median duration of SABR-aided systemic therapy.[67]

Dr. Chad Tang, Associate Professor, Department of Radiation Oncology, Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center

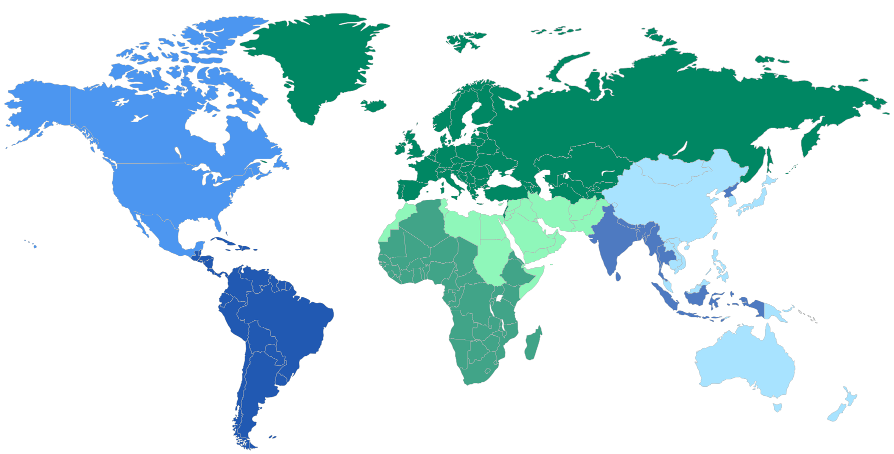
"For a long time there was consensus that RCC was radiation-resistant. The evolving understanding of the biology of these tumors and substantial improvements in RT technology have changed this perspective. With SBRT we can deliver very high doses of radiation with pinpoint accuracy, allowing us to control localized disease. The emerging data on RT in kidney cancer also is promising, and real-time imaging could address the intra-treatment motion that occurs as patients breathe, enabling better protection of healthy kidney tissue and nearby organs. This is especially important for patients who already have kidney dysfunction or have had their other kidney removed, because sparing healthy tissue is essential for preserving their remaining organ function.

With state-of-the-art imaging we also can identify very small metastases, allowing us to use SBRT to control metastatic renal cancer as well. A recent clinical study in which I participated showed that SBRT could delay the use of systemic therapy for about three years without compromising patients' overall survival. Importantly, patients in this study had much lower rates of toxicities than what we typically observe with systemic therapy. SBRT also is a more cost-effective option compared with the systemic therapy regimens typically used to treat metastatic RCC."

RT in head and neck cancer

RT can provide benefit in nearly 75% of patients with head and neck cancer.[70]

Head and neck cancer comprises cancers that begin in the mouth, throat, larynx, nasal sinuses, nasal cavity, and salivary glands.[71] Given the involvement of anatomic structures that have functional and cosmetic importance, treatment of head and neck cancer can be complex, and effectively dosing the tumor while protecting these organs can be challenging.[72,73] Radiation plays a key role in treating head and neck cancer and is used alone, in combination with chemotherapy, or after surgery in locoregionally advanced disease.[72] Re-irradiation also may be used to treat locoregional recurrence of head and neck cancer.[74,75] The type of radiation used depends on the location and stage of disease and the proximity of tumors to critical anatomic structures, and includes conventional IMRT, hypofractionated IMRT, SBRT, FLASH-RT, and proton therapy.[72]



- Western Pacific
- United States, Canada, and Mexico
- South-East Asia
- Americas (excluding United States, Canada, and Mexico)
- Eastern Mediterranean
- Africa
- Europe

Global incidence and mortality of head and neck cancer*[1]

Region	Incidence	Mortality	Mortality/ Incidence
South-East Asia	345,529	195,385	57%
Western Pacific	214,814	111,532	52%
Europe	176,895	79,367	45%
United States, Canada, and Mexico	74,736	18,180	24%
Americas (excluding United States, Canada, and Mexico)	51,049	25,778	50%
East Mediterranean	49,435	30,123	61%
Africa	34,479	21,943	64%

*Includes cancers of the lip, salivary glands, oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx

Changes in tumor volume and position relative to critical organs due to treatment response, weight and/or muscle loss, inflammation, and effects of radiation on nearby normal tissue also are a challenge in treating head and neck cancer.[76] A recent study showed that ART using CBCT tracking to identify and adapt therapy to anatomic changes reduced doses to critical salivary structures and the oral cavity.[37]

Benefits of ART in head and neck cancer

- ART can improve tumor targeting and minimize radiation exposure to healthy tissues.[73]
- ART can reduce doses to critical salivary structures and the oral cavity.[37]
- ART can improve locoregional control, survival rates, and side effects.[73]

Dr. Anthony Paravati, Executive Medical Director of Cancer Care and Chief of Radiation Oncology at Kettering Health

"RT offers the best chance of a definitive cure for head and neck tumors. Surgery may be curative in some cases, but it can be challenging to remove tumors without compromising patients' important functions such as speaking and swallowing. Systemic therapy can improve survival for some patients but is not curative on its own.

The evolution of RT technology has allowed us to eradicate primary head and neck tumors more effectively while modulating the dose away from sensitive anatomic structures. When I first began my training we were using 3D conformal RT and it was difficult to deliver the entire course of therapy without exposing the spinal cord. We had complicated, multimodal plans that increased the risk of side effects.

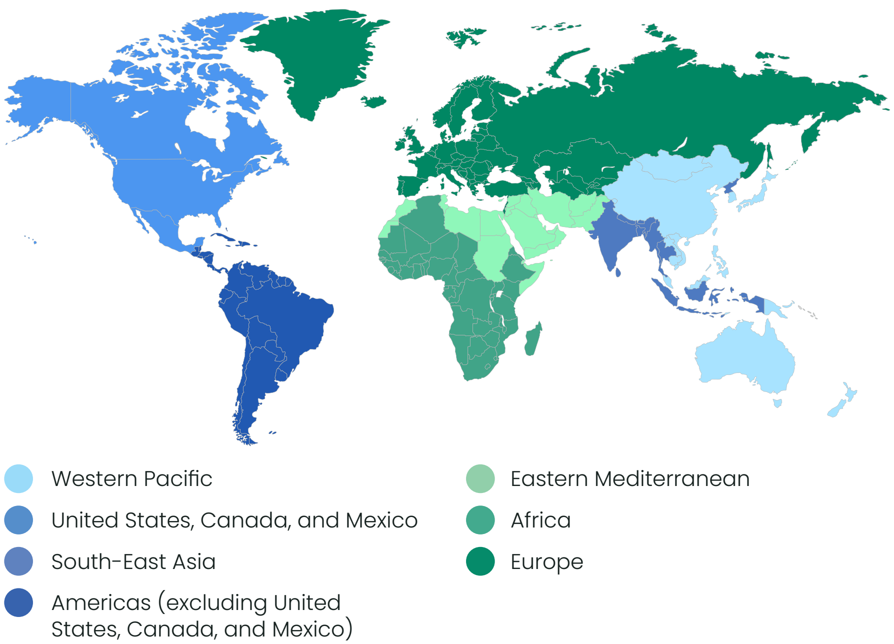
IMRT, proton therapy, and MRI-guided RT enable optimal tumor dosing and tissue sparing. ART can further increase this precision by adapting the plan over the course of therapy to lower overall exposure of normal tissue without sacrificing coverage of the tumor. This is important in head and neck cancer because patients can have rapid weight loss or dramatic tumor responses that alter the position of the tumor relative to critical anatomy. SBRT also is helping to improve outcomes in patients with recurrent tumors who require re-irradiation and aren't candidates for salvage therapy. I think continued technology advances will help even more patients achieve good outcomes."

RT in gynecologic cancers

Collectively, gynecologic cancers are the leading cause of cancer death in women globally.[1]

Gynecologic cancers include cancers of the cervix, uterus, ovaries, vagina, and vulva.[77] Of these cancers, cervical, uterine, and ovarian cancer are the most common and the most deadly.[1] RT plays an important role in the treatment of locally advanced cervical cancer, vaginal cancer, and recurrent uterine cancer and may be used in combination with surgery and/or systemic therapy.[78,79] Depending on the type and stage of disease, RT may include EBRT and brachytherapy alone or in combination with each other. Chemotherapy in combination with EBRT may be used to shrink tumors prior to brachytherapy for patients with locally advanced disease.

The availability of advanced RT techniques such as image-guided IMRT (IG-IMRT) and image-guided adaptive brachytherapy (IGABT) have helped to improve outcomes in some types of cervical cancer, inoperable uterine cancer, and vaginal cancer.[39,40,80-82]



Global incidence and mortality of gynecologic cancer*[1]

Region	Incidence	Mortality	Mortality/ Incidence
Western Pacific	400,322	145,931	36%
South-East Asia	315,405	186,496	59%
Europe	304,356	125,567	41%
Africa	155,643	97,439	63%
United States, Canada, and Mexico	144,539	48,010	33%
Americas (excluding United States, Canada, and Mexico)	105,352	50,618	48%
East Mediterranean	47,184	25,980	55%

*Includes cancers of the uterus, cervix, ovaries, vagina, vulva

Benefits of image-guided ART in gynecologic cancers

- A regimen of IG-IMRT, concurrent cisplatin chemotherapy, and MRI-guided IGABT showed high rates of overall survival and local control with low rates of grade 3-5 side effects in locally advanced cervical cancer.[40]
- EBRT followed by a 3D-IGABT boost is used to treat inoperable uterine cancer.[81]
- MRI-guided brachytherapy demonstrated high rates of local control with limited side effects in primary vaginal cancer.[82]
- Use of MR-linac as an MR simulator for brachytherapy may help to increase access to personalized RT for gynecologic cancers.[83]

Dr. Akila Viswanathan, Chair, Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University School of Medicine

"Delivering an effective dose to gynecologic tumors while protecting the bladder, adjacent bowel, and other normal structures within the pelvis can be difficult. Advanced imaging technologies make it easier to position brachytherapy catheters for optimal efficacy and safety.

Early in my career I was one of just two clinicians in the United States using MRI after brachytherapy placement to guide treatment planning, and soon became the only radiation oncologist doing real-time MRI-guided insertions in an interventional MRI suite. It took nearly a decade before MRI in cervical cancer was adopted more widely. Initially MRI was used to identify catheter location after placement, with the radiation dose then calculated based on catheter position. Today, we can develop an optimized dose plan based on a pre-treatment MRI and then ensure that the catheters are placed in the tumor according to the plan using real-time MRI during the procedure. This tailors treatment to each patient's tumor.

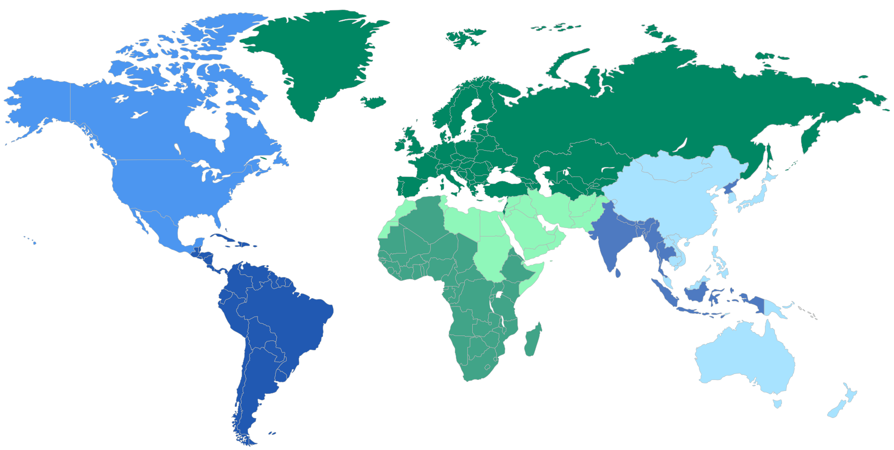
My initial experience with real-time MRI-guided brachytherapy used an interventional MRI system run by one of the institution's neurosurgeons. The limited availability of MRI scanners in RT departments can be an obstacle to broader use of MRI-guided brachytherapy in the treatment of gynecologic cancers. MR-linacs have shown promise when used as simulators to plan high-dose rate gynecologic brachytherapy, which could help increase access to personalized, precision brachytherapy for several gynecologic cancers."

RT in pancreatic cancer

The global burden of pancreatic cancer is rising.[84]

Surgery can potentially cure pancreatic cancer but 80-85% of newly diagnosed patients are ineligible for it due to advanced disease.[85] Chemotherapy may be used before or after surgery and also is used in patients who aren't candidates for surgery or have metastatic disease.[85] Radiation therapy may be used to treat locally advanced disease for patients with inoperable tumors that have not metastasized.[85]

The position of the pancreas in close proximity to multiple critical organs has made the safe use of RT in pancreatic cancer a challenge. Increased precision in RT dosing is helping overcome this challenge. A number of studies support the potential of SBRT in patients with locally advanced pancreatic cancer.[86] Several studies have shown that SBRT in combination with chemotherapy was non-inferior for overall survival, had higher rates of local control, had improved 2-year overall survival, and reduced acute side effects compared with conventional RT combined with chemotherapy.[87,88] ART also is showing promise in improving overall survival and reducing side effects.[36] Use of customized MRI images that provide enhanced



Global incidence and mortality of pancreatic cancer[1]

Region	Incidence	Mortality	Mortality/ Incidence
Western Pacific	187,708	168,979	90%
Europe	160,412	151,993	95%
United States, Canada, and Mexico	72,888	61,292	84%
Americas (excluding United States, Canada, and Mexico)	35,122	32,973	94%
South-East Asia	27,335	26,344	96%
East Mediterranean	14,115	13,379	95%
Africa	13,213	12,269	93%

anatomic visualization (known as T1-weighted, or T1w, images) can improve visualization, enabling margin reductions and sparing organs near the pancreas during MRI-guided SBRT.[89]

ART in pancreatic cancer

- Online ART-based SBRT enhanced dose distribution to the target volume while reducing exposure to critical organs.[90]
- ART improved overall survival time and rates of 2-year survival, 2-year local control, and 2-year disease-free progression compared with results typically achieved with non-adaptive RT in patients with borderline resectable or locally advanced pancreatic cancer.[36]

Dr. Lauren Henke, Associate Professor of Radiation Oncology, University Hospitals, Case Western Reserve University and Director, GI Radiation Oncology, Seidman Cancer Center

"Historically, conventional RT has been associated with high rates of grade 3 toxicities without a convincing benefit in terms of survival or local control. The challenge has been to deliver ablative doses to a tumor that is surrounded by multiple critical organs that move from day to day and during treatment as the patient breathes, such as the stomach and the intestine.

Innovations in three different areas have helped to overcome that challenge. Today, we have unprecedented on-board image quality, which is radically different from the imaging available when I started my residency. And that image clarity has enabled important advances in treatment planning. Not that long ago it took days to generate high-quality IMRT, VMAT, and SBRT plans—now it takes minutes, where we can adjust a plan even on the fly. Third, we now have motion management systems that allow us to dose the pancreas safely.

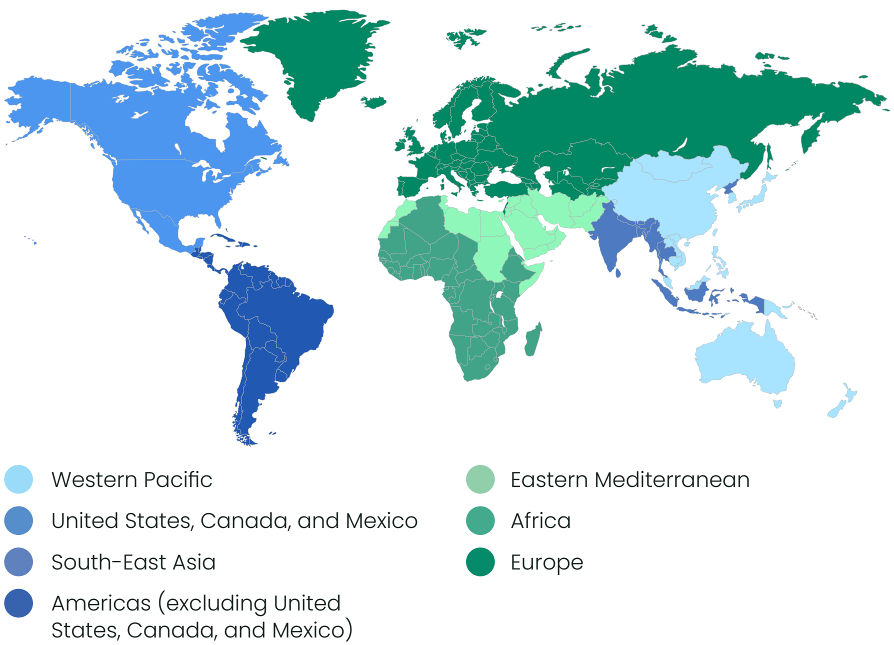
With these innovations, we can now use RT across the continuum of pancreatic cancer. As an example, on one recent day I saw patients at four different stages of disease and all of them are being treated with RT. One had a stage I tumor that was medically inoperable due to comorbidities. Then I saw a patient with a borderline resectable tumor who was getting RT ahead of surgery and one who had just had surgery and needed RT for a positive margin. And then I saw a patient who was receiving RT for palliation of pain in very late-stage disease. This is an important evolution in a relatively short period of time, and I'm glad that I'm able to play a role in developing new technologies that, hopefully, will further improve treatment."

RT in breast cancer

Breast cancer is the most commonly diagnosed cancer and leading cause of cancer death globally in women.[1]

Multiple therapeutic approaches are used in the treatment of breast cancer, including surgery, RT, chemotherapy, hormone therapy, targeted therapy, and immunotherapy.[91] RT can be used to reduce the risk of recurrence following breast-conserving surgery (BCS, also called lumpectomy) and, in some patients, may also be used after mastectomy.[92] It also may be used to treat breast cancer that has spread to other parts of the body.[92] Recent studies suggest that SBRT administered prior to surgery may help to reduce overall treatment time and may also shrink tumors sufficiently to allow BCS rather than mastectomy.[93] SBRT may also be a good option for primary breast tumors in women unable to undergo surgery and for a variety of breast cancer stages in elderly women.[94,95]

While EBRT is the most common form of RT used in breast cancer, brachytherapy may also be used following BCS.[92] An ongoing clinical study is evaluating proton therapy as a heart-sparing approach to RT in breast cancer.[96] ART also shows



Global incidence and mortality of breast cancer[1]

Region	Incidence	Mortality	Mortality/ Incidence
Europe	604,941	160,043	26%
Western Pacific	575,281	128,728	22%
United States, Canada, and Mexico	337,241	57,922	17%
South-East Asia	313,537	142,986	46%
Americas (excluding United States, Canada, and Mexico)	188,641	51,506	27%
Africa	146,130	71,662	49%
East Mediterranean	130,062	52,836	41%

promise in several aspects of breast RT, including enabling more precise dosing of RT boost, reducing margins, and minimizing dosing to healthy tissue.[97,98] One study found that lumpectomy cavity size (the space remaining after tumor removal in BCS) decreased a median of 27% over the duration of treatment, and that plans adapted daily better met pre-specified treatment goals compared with scheduled plans as cavity size changed over time.[99] Real-time tracking and gating may also have benefit in addressing intrafraction motion that results from breathing and heart contraction, improving dosing to the tumor while protecting critical organs. This is especially challenging in tumors of the left breast given their proximity to the heart.

Advances in breast cancer RT

- For women with early-stage breast cancer, RT after surgery (BCS or mastectomy) a lower dose (26 Gy) can be delivered in 5 sessions over 1 week without increased risk of recurrence or side effects compared with 40 Gy delivered in 15 sessions over 3 weeks.[100]
- For women with invasive breast cancer who require RT to the armpit following surgery, 26 Gy delivered in 5 sessions over 1 week is as safe as 40 Gy delivered in 15 sessions over 3 weeks.[101]
- Ongoing research is evaluating a 5-fraction regimen that includes a "boost" for women with higher risk breast cancer[102] and proton therapy as a heart-sparing RT approach.[96]

Professor Anna Kirby, Consultant Clinical Oncologist, The Royal Marsden and Institute of Cancer Research

"When I first started practicing, one of my first clinics was reviewing patients who were undergoing RT for breast cancer. Nearly every one of these patients experienced obvious toxicity, such as peeling of the skin under the armpit, changes to the skin on the breast, and shrinkage or changes in firmness of the breast itself. Given that treatment planning at that time was done only in two dimensions, it's not surprising that so many women experienced these adverse RT effects.

Over the last two decades, RT has evolved to become a safer, more effective, and gentler treatment that is tailored, precision therapy. The use of CT imaging and 3D planning have allowed us to carefully deliver dose to the at-risk tissues while sparing critical organs, especially the heart. Hypofractionated regimens have also made treatment less burdensome for patients while providing excellent outcomes. I have been involved in a clinical study—FAST Forward—that showed we could reduce the total dose and the number of treatment sessions without compromising long-term safety or efficacy outcomes in women undergoing RT to the breast after BCS or mastectomy. Receiving treatment in 5 sessions over one week rather than 15 sessions over three weeks minimizes patients' stress, inconvenience, and cost of care. Importantly, fewer sessions per patient allows us to treat more patients each month, which is critical for expanding access to cutting-edge care."

Innovation on the horizon

A 125-year old therapy with unlimited future potential.

Ongoing innovation continues to make RT safer, more effective, and more convenient. Here are just a few of the many exciting innovations and areas of exploration making the next impact on the evolution of RT.

Dr. Alison Tree, Consultant Clinical Oncologist, The Royal Marsden NHS Foundation Trust and Honorary Reader, Institute of Cancer Research

"Our center participated in DESTINATION-1, a trial designed to de-escalate dosing to healthy prostate tissue when treating prostate cancer with five-fraction SBRT. We, in collaboration with partners across the MR-Linac Consortium, are now recruiting patients for DESTINATION-2, which will compare uniform versus de-escalated dosing with a two-fraction regimen. The results of these trials will help us understand how de-escalation can be used to reduce toxicity without compromising efficacy in prostate cancer."

Dr. Percy Lee, Professor and Vice Chair of Clinical Research, Department of Radiation Oncology and Medical Director of Orange County & Coastal Region Radiation Oncology, City of Hope

"FLASH-RT, in which a full dose of RT is delivered in less than 200-300 milliseconds, has demonstrated interesting results in animal models and early clinical studies. I can imagine the day when we do single-fraction treatment with FLASH-RT, providing better efficacy with less toxicity and much greater efficiency."

Dr. Ariane Lapierre, MD, PhD, Deputy Head of Radiation Oncology, Hospices Civils de Lyon, France

"Low oxygen (hypoxia) in tumor cells is a major factor in resistance to RT. Our center is developing maps that show how hypoxia changes in different areas of a patient's tumor from day to day. We can then use these maps to study the relationship between hypoxia and RT resistance. In the future these maps may allow us to further adapt dosing based on tumor biology."

Prof. Filippo Alongi - Professor of Radiation Oncology, University of Brescia and Chair/Director of Advanced Radiation Oncology, IRCCS Ospedale Sacro Cuore-Don Calabria, Italy

"Our ability to deliver ablative doses of radiation with high precision is making it possible to treat—and even cure—oligometastatic disease by simultaneously eliminating multiple lesions in one or just a few daily sessions. In most cases this can be achieved without significant side effects. It also can be used for long-term control of oligoprogressive disease, ablating lesions that don't respond to systemic therapy. This non-invasive and safe approach can delay the use of second- or third-line systemic therapies, allowing them to be used to control disease if needed later in treatment."

Prof. Dr. med. Dr. Esther Troost, Chair of Department of Radiotherapy and Radiation Oncology, University Hospital and Faculty of Medicine Carl Gustav Carus, Technische Universität Dresden (UKD)

"The precision dosing and tissue sparing capabilities of MRI-integrated photon systems are milestones in treating tumors arising from soft tissues. MRI-guided proton therapy may further improve efficacy and safety by increasing precision and reducing the dose. Our center has been working on the latter concept for the last 10 years and we hope to bring it to clinical studies shortly."

Dr. Laura Dawson, Professor and Chair, Department of Radiation Oncology, University of Toronto and Radiation Oncologist, Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada

"A few years ago, many of the cancer treatment guidelines still didn't have RT recommended for treating liver cancer, even though the technology was available. Today, many international and national treatment guidelines include strong recommendations for the use of RT in patients with liver tumors. This is a very important change."

The need for RT today exceeds its availability

There are significant inequities in RT access. While most high-income countries have one radiation therapy unit available for every 130,600 people, a single unit must provide service for 1-5 million people in low- and middle-income countries (LMICs) and more than 15 million people in low-income countries.[103]

Approximately 23 LMICs with populations over 1 million are without a single RT treatment site.[104] Due to these disparities, it is estimated that LMICs have only 34% of global RT equipment while comprising 80% of the global population.[103] The gap between the demand and availability of RT in LMICs has widened over the past decade and is expected to grow over the next 15 years.[105]

Expanding access to RT also requires increasing the number of trained RT professionals. It was estimated that, in 2022, there were fewer radiation oncologists, radiation therapists, and medical physicists than needed globally, and 71% of countries did not have enough radiation oncologists to meet the demands for basic RT.[106] The anticipated need for an even greater number of RT professionals in 2050 suggests that demand will continue to outpace capacity without urgent action.[106]

“Democratizing access to RT is about more than simply installing additional RT devices. As a technology-based therapy, the safe and effective use of RT requires infrastructure such as reliable energy sources, high-speed data connectivity, and specialized construction. Just as a smart phone isn’t “smart” without data connectivity and specialized apps, an RT device by itself can’t deliver the care cancer patients need. Investing in RT also drives investment in critical infrastructure that has benefits beyond healthcare and spurs economic development. Prioritizing these investments can be beneficial to a country’s health as well as its wealth.”

— Prof. Pat Price, Clinical Oncologist, Founder and Chair of Radiotherapy UK, Visiting Professor Department of Surgery and Cancer, Imperial College London, Co-Founder and Chair of the Global Coalition for Radiotherapy

Increased RT access can save lives and money

With an estimated additional 6.5-8.4 million cancer patients needing RT by 2050,[106] the need for advanced technologies that can increase overall treatment capacity by reducing treatment times is a global health challenge.

Broader availability of hypofractionated regimens can lower the cost of RT, reduce treatment time, and increase access to care while providing effective therapy.[103] Thus, increasing access to the technologies that enable these regimens should be a priority.

Democratizing access to RT is a global challenge that requires a global solution. Collaboration—among governments, industry, academia, non-government organizations, clinicians, and patients—is the foundation on which to build the RT capacity and innovation that cancer patients need to feel better and live longer.

Hypofractionated regimens save lives and money

Wider adoption of hypofractionated regimens for prostate and breast cancer would enable a reduction of 36.2 million fractions annually, translating to an additional 2.2 million patients treated in these indications.[103] Replacing 80% or 50% of conventional breast and prostate RT with hypofractionated regimens could save US$4.41 billion and US$2.76 billion, respectively.[103]

Beyond cancer

In the early days of RT, this then-novel therapy primarily was used to treat a spectrum of non-cancer indications, an approach that has continued in German-speaking countries for more than 100 years.[107]

The excellent efficacy and safety profiles of today's advanced RT technologies have led to a renewed interest in using RT to treat a variety of cardiac diseases and soft tissue, musculoskeletal, and neurological disorders.[108] Several studies suggest that low-dose RT (LDRT) offers a non-invasive and cost-effective approach that can reduce pain and improve function in patients with osteoarthritis.[109,110] An early-stage clinical study showed that Stereotactic Arrhythmia Radioablation (STAR) using SBRT can reduce the number of arrhythmic events and use of antiarrhythmic medications and improve quality of life in patients with ventricular tachycardia.[111] Another study suggested that cardiorespiratory motion-related radiation dosing uncertainty during STAR could be addressed by using an MR-linac system equipped with real-time motion management.[112] Ongoing research will help to inform our understanding of the role that RT may play in improving outcomes for patients with diseases other than cancer.

125 years after its first therapeutic use, the research and clinical communities continue to identify new ways to deploy RT to benefit patients. Supporting, prioritizing, and investing in basic and translational science is critical to writing the next chapter in the evolving RT story. The discoveries we make today become the therapies that help patients have more and better tomorrows.

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Glossary

ART – Adaptive RT: Advanced forms of RT in which treatment is adapted over the course of therapy and/or during individual treatment sessions

CBCT - Cone-Beam CT: Uses lower-energy x-rays, allows 3D images to be captured during each treatment session without increasing the risk of imaging-related radiation

CSS - Cancer-Specific Survival: Survival related to a patient's cancer (excludes death from causes unrelated to cancer)

CT - Computed Tomography: Captures multiple images using x-rays, which are then combined to create higher-resolution, 3D models of the the patient's anatomy

CTV - Clinical Tumor Volume: Clinical Tumor Volume: Includes the GTV plus an additional margin around the tumor to include tumor cells that may not appear on imaging

EBRT – External beam radiation therapy: Radiation source is outside the body

GTV - Gross Tumor Volume: Volume of the tumor defined by imaging studies

GU - Genitourinary: The genital and urinary systems

Gy – Gray: The unit in radiation therapy used to measure the amount of energy from radiation absorbed in tissues

G2 – Grade 2: Moderate side effects

HGG - High Grade Gliomas: A type of aggressive brain cancer

IMRT - Intensity Modulated RT: Enables more precise targeting of radiation, with higher doses delivered to the tumor and reduced dosing to surrounding tissue

MRI - Magnetic Resonance Imaging: A technique that uses powerful magnets to create detailed images of structures and tissues inside the body

NSCLC - Non-Small Cell Lung Cancer: Cancer of the epithelial lining of the lungs

OS – Overall Survival: How long the patient survives from diagnosis or treatment initiation until the patient's death

PET – Positron Emission Tomography: An imaging approach that uses radioactive tracers to visualize organ and tissue function within the body

PFS – Progression Free Survival: How long the patient survives without disease progression

PTV - Planning Tumor Volume: Includes the CTV plus an additional margin to account for potential movement during treatment delivery

PULSAR - Personalized Ultra-fractionated Stereotactic Adaptive Radiotherapy: An advanced form of EBRT in which very high doses of radiation are delivered at much longer intervals (weeks or months) than current regimens

RCC - Renal Cell Carcinoma: Cancer of cells in the kidney

RT – Radiation Therapy: The use of beams of radiation or particles to treat disease

SABR – Stereotactic Ablative Body Radiotherapy: An advanced form of EBRT that allows treatment to be delivered in 1-5 fractions (also known as Stereotactic Body Radiation Therapy [SBRT])

SBRT - Stereotactic Body Radiation Therapy: An advanced form of EBRT that allows treatment to be delivered in 1-5 fractions (also known as Stereotactic Ablative Radiation Therapy [SABR])

SRS - Stereotactic Radiosurgery: Uses multiple beams to target tumors in the brain in a single fraction

SRT - Stereotactic RT: Includes SRS and SBRT

STFS - Systemic Therapy-Free Survival: Period of time during which a patient does not require the use of systemic therapy

VMAT - Volumetric Modulated Arc Therapy: An advanced form of IMRT that delivers radiation with a beam that moves in arc around the patient rather than firing the beam multiple times from different directions

About Adaptive

To learn more about adaptive radiotherapy, please visit
www.AboutAdaptive.com