MRIdian® MR-Guided Radiation Therapy for Pancreatic Cancer

Overview

Pancreatic cancer is among the deadliest cancers. While incidence is comparatively low—it's the twelfth most common type of cancer diagnosed worldwide[1]—mortality is high, with most patients succumbing to their disease within one year of diagnosis.[2] In Europe, the median survival after diagnosis is just 4.6 months.[2] The five-year overall survival rate for pancreatic cancer is eight percent, which is among the lowest for any cancer type.[3] More than half of diagnoses occur after the cancer has metastasized, when the five-year relative survival rate drops to 2.9 percent.[4]

Worldwide Pancreatic Cancer Statistics[1]

- Twelfth most common cancer type
- 458,918 new cases each year
- 432,242 deaths annually

U.S. Pancreatic Cancer Statistics[4]

- Eleventh most common cancer
- Third leading cause of cancer death with an estimated 47,050 deaths in 2020
- 57,600 new diagnoses in 2020

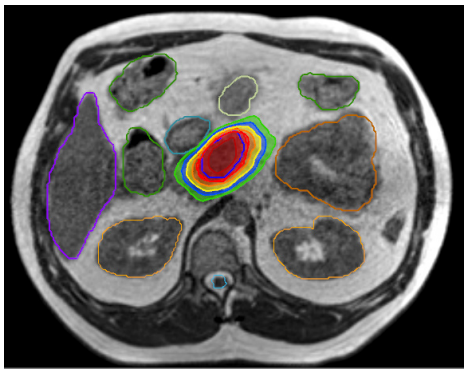
Treatment Landscape & Challenges

Current treatment options for pancreatic cancer include surgery, chemotherapy, and radiation therapy. The majority of patients are diagnosed with either locally advanced disease and/or distant metastases and are not candidates for surgery. Treatment offered to this population is limited to multi-agent chemotherapy and various schedules of radiation therapy.

Shortened radiation courses, including stereotactic body radiation therapy (SBRT), have emerged as promising options for patients with locally advanced pancreatic cancer (LAPC); however, delivery of high ablative radiation doses for pancreatic cancer has traditionally been challenging due to the proximity of nearby critical structures including the duodenum, small bowel, stomach, large bowel, liver, and kidneys. Planning target volume (PTV) setup margins frequently overlap with these organs, putting these critical structures at risk for radiation damage. Soft-tissue visualization with CT-based image guidance is limited. Additional challenges include respiratory organ motion and interfraction changes in the stomach and bowel filling and position.

However, recent studies have demonstrated promising results delivering high-dose, ablative radiation therapy with MR-guidance and daily on-table adaptive dose planning, which, when combined, help mitigate the visualization and motion management obstacles.

The American Society for Radiation Oncology (ASTRO) recently developed its first clinical guideline on the role of radiation therapy in pancreatic cancer treatment, which differentiates between conventionally fractionated radiation therapy and SBRT, providing the first clinical guidance on shortened treatment delivery. The guideline highlights the value of technical advances in respiratory motion assessment, respiratory management, and treatment planning and delivery, promising local tumor control, maintenance of quality of life, and reduced toxicity rates of SBRT for pancreatic cancer.[5]



MRIdian image of pancreas tumor with contours and dose applied

PANCREATIC CANCER

The MRIdian Advantage

MRIdian offers precise and accurately controlled radiation delivery with MR-guidance—the ability for on-table adaptive replanning—and real-time, soft-tissue-tracking-based, automated beam control. MRIdian's ability to see the tumor and surrounding structures, adapt the treatment to any change in the position and size of the target and surrounding healthy tissue, and track the tumor in real-time, automatically gating the beam as needed, allows for more precise radiation therapy and minimizes radiation dose to surrounding critical structures. In the treatment of pancreatic cancer, these unique capabilities enable:

- High-contrast, high-resolution MR soft tissue imaging, unachievable with conventional IGRT
- Clinical confidence to escalate radiation doses safely and shorten treatment courses (hypofractionated treatments)
  - Potential to reduce toxicity and extend survival and quality of life, as early findings suggest
- On-table adaptive therapy, which allows clinicians to customize the radiation treatment plan on a daily basis as needed to maintain the physician's dose-prescription intent; intrafraction, automated, real-time, imaging-based beam control allows delivery of the radiation dose precisely to the target while reliably avoiding organs at risk
  - Daily plan re-optimization with real-time beam control may allow for tighter margins and maximal normal tissue sparing
- Real-time, MR-imaging-based intrafraction motion management to address respiratory motion
- Elimination of need to implant fiducial markers, thereby avoiding an invasive procedure, avoiding potential risk of associated complications and costs, and reducing the delay in treatment initiation associated with placement of fiducials
- May provide a treatment option for patients who otherwise would not be offered treatment
- Reduced burden on the patient, with only five treatment sessions needed, as compared to conventional radiotherapy which requires ~28 treatments

Ongoing Clinical Trials

Compelling data from the recent multi-center retrospective study *(see below)* prompted the development of a larger Phase 2 clinical trial aimed at investigating in a controlled, prospective manner the robustness of this outcome, and to track quality of life over a five-year trial period.

Eligible Participants: Patients with borderline resectable or inoperable locally advanced pancreatic cancer who are 18 years and older and meet the inclusion and exclusion criteria noted within the study description.

Trial Design: In this single-arm study, participants will receive radiation therapy using integrated magnetic resonance imaging (ViewRay's MRIdian MR-Guided Radiation Therapy System) at a dose of 50 Gray in 5 fractions (treatment sessions). Fractions will be delivered at least twice per week and with at least 18 hours between treatments. Each participant will be aligned in the treatment system with MRI-guidance. On-table adaptive replanning will be used when clinically indicated. In all patients, real-time MR-imaging will be used throughout treatment delivery to monitor the target location and control the radiation beam, as necessary.

Outcome Measures: The primary outcome measure of the study is grade 3 or higher gastrointestinal toxicity in the first 90 days after treatment. Secondary measures include overall survival at two years, distant progression-free survival at six months and changes in patient reported quality of life (pre-treatment to 12 months post-treatment and for longer periods up to five years).

For more information about trial design, inclusion and exclusion criteria, and trial locations visit https://clinicaltrials.gov/ct2/show/NCT03621644.

Noteworthy Clinical Findings

A recent multi-center retrospective study of 44 patients at five MRIdian centers showed that high-dose, adaptive treatment improved overall survival and eliminated serious toxicity in pancreatic cancer patients.

Study Specifics

- Patients with inoperable pancreatic cancer treated with MRgRT
- Patients were split into high-dose BED_{10} > 70 Gy and standard-dose BED_{10} ≤ 70 Gy groups
- Adapted fractions (83% high-dose, 15% standard-dose)

Key Findings

- Median survival was 20.8 months high-dose vs. 10.8 months standard-dose
- Overall survival was statistically significantly higher in high-dose group (49% vs. 30% at 2 years) (P = 0.03)
- Grade 3+ GI toxicity was 0% in high-dose and 15% in standard-dose groups

Study published in the May 2019 edition of Cancer Medicine.[6]

Supporting Peer-Reviewed Publications

Bohoudi, O., Bruynzeel, A. M. E., Senan, S., Cuijpers, J. P., Slotman, B. J., Lagerwaard, F. J., et al. (2017). Fast and robust online adaptive planning in stereotactic MR-guided adaptive radiation therapy (SMART) for pancreatic cancer. Radiotherapy and Oncology, 125(3), 439–444.

El-Bared, N., Portelance, L., Spieler, B. O., Kwon, D., Padgett, K. R., Brown, K. M., et al. (2019). Dosimetric benefits and practical pitfalls of daily online adaptive MRI-guided stereotactic radiation therapy for pancreatic cancer. Practical Radiation Oncology, 9(1), e46–e54.

Lee, P., Luterstein, E., Raldow, A., Kishan, A. U., Kalbasi, A., Beron, P. J., et al. (2018). Clinical outcomes using stereotactic MRI-guided adaptive radiation therapy (SMART) for primary and metastatic abdominal and pelvic tumors. International Journal of Radiation Oncology • Biology • Physics, 102(3 Suppl), E66–E67.

Luterstein, E., Cao, M., Lamb, J., Raldow, A. C., Low, D. A., Steinberg, M. L., et al. (2018). Stereotactic MRI-guided adaptive radiation therapy (SMART) for locally advanced pancreatic cancer: a promising approach. Cureus, 10(3), e2324.

Olberg, S., Green, O., Cai, B., Yang, D., Rodriguez, V., Zhang, H., et al. (2018). Optimization of treatment planning workflow and tumor coverage during daily adaptive magnetic resonance image guided radiation therapy (MR-IGRT) of pancreatic cancer. Radiation Oncology, 13(1), 51.

Parikh, P. J., Roach Jr., M. C., Green, O. L., Kashani, R., Rudra, S., Henke, L. E., et al. (2018). Outcomes of two 100 Gy BED radiation regimens for inoperable pancreas cancer. International Journal of Radiation Oncology • Biology • Physics, 102(3 Suppl), E79–E80.

Ramey, S. J., Padgett, K. R., Lamichhane, N., Neboori, H. J., Kwon, D., Mellon, E. A., et al. (2018). Dosimetric analysis of stereotactic body radiation therapy for pancreatic cancer using MR-guided tri-60Co unit, MR-guided LINAC, and conventional LINAC-based plans. Practical Radiation Oncology, 8(5), e312–e321.

Rudra, S., Jiang, N., Rosenberg, S. A., Olsen, J. R., Roach, M. C., Wan, L., et al. (2019). Using adaptive magnetic resonance image-guided radiation therapy for treatment of inoperable pancreatic cancer. Cancer Medicine, 8(5), 2123–2132.

Tyran, M., Jiang, N., Cao, M., Raldow, A., Lamb, J. M., Low, D., et al. (2018). Retrospective evaluation of decision-making for pancreatic stereotactic MR-guided adaptive radiotherapy. Radiotherapy and Oncology, 129(2), 319–325.

van Sornsen de Koste, J. R., Palacios, M. A., Bruynzeel, A. M. E., Slotman, B. J., Senan, S., Lagerwaard, F. J. (2018). MR-guided gated stereotactic radiation therapy delivery for lung, adrenal, and pancreatic tumors: a geometric analysis. International Journal of Radiation Oncology • Biology • Physics, 102(4), 858–866.

Supporting Presentations & Videos

High Dose, On-Table, Adaptive Radiation Therapy for Pancreatic Cancer: Encouraging Early Results
Michael Bassetti, MD, PhD
University of Wisconsin, Carbone Cancer Center
https://vimeo.com/293472071

MR-Guided SBRT for Pancreas With On-Table Adaptation on MRIdian – MCI Experience
Michael Chuong, MD
Miami Cancer Institute, Baptist Health South Florida
https://vimeo.com/368137984

Prospective Experience With Real-Time Online Adaptive Radiotherapy for Abdominal and Pelvic Malignancies
Lauren Henke, MD
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine
https://vimeo.com/298626732

SMART: Status Update on the First Prospective, Multi-Institutional Study on Ablative Pancreas SBRT
Parag Parikh, MD
Henry Ford Health System
https://vimeo.com/362615286

Improving Pancreatic Cancer Survival by Using MR-Guided Adaptive Radiation
Parag Parikh, BSE, MD
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine – St. Louis, MO
https://vimeo.com/235284105

References:

[1]Ferlay, J., et al. (2018). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Retrieved August 30, 2019 from https://gco.iarc.fr/today

[2]United European Gastroenterology. (2018). Pancreatic cancer across Europe: Taking a united stand. Retrieved May 5, 2020 from https://www.spg.pt/wp-content/uploads/2018/11/Pancreatic_Cancer_Report.pdf

[3]Pancreatica. Pancreatic Cancer Topics: Pancreatic Prognosis and Survival. Retrieved from https://pancreatica.org/pancreatic-cancer/pancreatic-cancer-prognosis/

[4]National Cancer Institute: Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Pancreatic Cancer. Retrieved from https://seer.cancer.gov/statfacts/html/pancreas.html

[5]American Society of Radiation Oncology. (2019). New guideline clarified role of radiation therapy in pancreatic cancer treatment. Retrieved May 5, 2020 from https://www.astro.org/News-and-Publications/News-and-Media-Center/News-Releases/2019/New-guideline-clarifies-role-of-radiation-therapy

[6]Rudra, S., Jiang, N., Rosenberg, S. A., Olsen, J. R., Roach, M. C., Wan, L., et al. (2019). Using adaptive magnetic resonance image-guided radiation therapy for treatment of inoperable pancreatic cancer. Cancer Medicine, 8(5), 2123–2132.

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