



Starting Radiotherapy in hours instead of weeks

Accelerating the path to treatment to maximize agility and impact

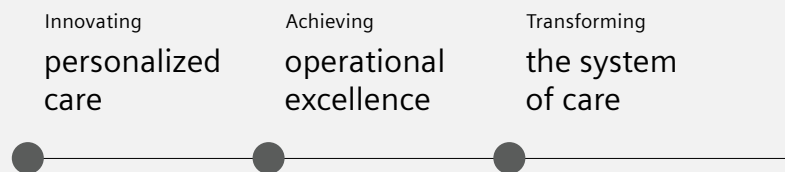
A thought leadership paper on "Innovating personalized care"

Preface

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Executive summary

Patients who have to undergo radiation as part of their cancer therapy often have to wait weeks if not months to begin. Medical literature suggests that longer waiting times sometimes correlate with worse outcomes. In recent years, radiation cancer treatment programs have become shorter and the efficiency of workflows has been enhanced through better planning software, digitalization and automation of processes that significantly reduce the number of steps and the order of tasks. Yet, radically shortening time to radiotherapy treatment remains a stubborn obstacle.

This paper looks at the reasons for these delays after diagnoses and analyzes the benefits of shortening time-to-treatment initiation. These include significant medical benefits (e.g., better outcomes for different types of cancer); benefits to patients and their families in terms of reduced anxiety and disruption, as well as enhanced feelings of control of their situation; and benefits to healthcare providers, specifically in terms of improved efficiencies, reduced overhead, and lower patient attrition.

Finally, this paper presents a review of a world-leading innovative initiative at Amsterdam UMC Cancer Center in the Netherlands, which is achieving the goal of same-day treatment for radiation oncology—reducing the time between consultation and start of treatment to as little as two hours for a selected group of patients treated for painful tumors.

The challenge




Throughout the cancer care community, one point on which everyone agrees is that time is critical. A difference of several weeks, or even days, can have a profound impact on the effectiveness of treatment, on the well-being of patients and their families, and on the costs and complexity of care. Every four weeks of delay in cancer treatment raises the risk of death by approximately 10%. Minimizing delays to treatment could improve cancer survival rates.¹

Delays along the cancer care pathway are, unfortunately, the norm. Cancer treatment delay is a problem in health systems worldwide; it is not unique to poorly funded healthcare systems, low-income regions, or remote communities. In the UK, delays of up to two months are common.²

NHS statistics released in June 2022 indicate that 79% of cancer patients receiving an urgent referral for suspected cancer are seen by a specialist within two weeks. While this is encouraging, it still means that more than 21% of patients receiving an urgent referral are not seen for more than two weeks. For patients suffering from breast cancer symptoms, just over 60% are seen within two weeks of referral; but again, this means that more than a third of women with breast cancer symptoms are unable to see a specialist for more than two weeks.²

In the U.S. the situation is not significantly better. An analysis of SEER-Medicare data concluded that more than 50% of patients with head and neck squamous cell carcinoma who undergo surgery and post operative radiotherapy receive care that does not adhere to National Comprehensive Cancer Network guidelines that recommend initiating post operative radiotherapy within 6 weeks of surgery.^{3,4}

Cancer care: UK diagnosis and treatment targets and real-world examples ⁵

 62 day target When cancer is first suspected, everyone should have a confirmed diagnosis and start treatment within 62 days.	 28 day target A patient should not wait more than 28 days from referral to finding out whether they have cancer or not (point of diagnosis).	 31 day target A patient should not have to wait more than 31 days from diagnosis to the start of treatment.
Real impact on patients: Every month delay in cancer treatment can raise risk of death by around 10%.	UK (according to NHS): Delays up to 2 months 21% of cancer patients who receive an urgent referral for suspected cancer are not seen by a specialist within 2 weeks . 40% of patients suffering from breast cancer symptoms are not seen by a specialist within 2 weeks of referral.	US: >50% of patients with head and neck squamous cell carcinoma who undergo surgery and post operative radiotherapy receive care later than 6 weeks after surgery, which does not adhere to the NCCN guidelines.

“Perhaps the most troubling part, even for the most advanced centers, is that very few departments, if any, can tell patients when exactly their treatment will start. There is a large amount of uncertainty in the process and patient anxiety and attrition is a common problem.”

Sasa Mutic, PhD
Senior Vice President, Varian

Delays have real impact

Delays are more than an organizational inconvenience. Delay in timely access to radiotherapy allows cancers to progress and become unsuitable for radical treatment, compromises treatment options and results in decreased cure rates and worse patient outcomes. Delays also negatively impact the psychological well-being of patients and place unnecessary burdens on hospitals and healthcare systems.

Patients

The greatest risk from delays in time to treatment initiation is that patient outcomes can be compromised. Earlier treatment can focus more strongly on curative intent, increasing the likelihood that the cancer can be treated effectively or even cured. The correlation between early cancer treatment and more positive outcomes is well known. And delays in radiotherapy following surgery are known to increase the risk of local recurrence of the cancer.⁶ For head and neck cancer patients, a treatment delay or interruption of even one day can decrease the local control* rate by 1.4%.⁷

For early-stage breast, lung, renal, and pancreatic cancers in curative settings, delays in time-to-treatment initiation can increase the risk of mortality by up to 3.2% per week.⁸

In some cases, patients suffer from cancer types that require immediate attention, for example some leukemias, lymphomas, or certain other types of cancer that can be aggressive, growing and spreading quickly. In other cases, a tumor may be pressing on another organ or vital body part and quick treatment is necessary to relieve



Accelerated path to treatment is most relevant for patients with

- Relevant clinical symptoms and indication for RT
- Highly aggressive tumors, with a risk of progression in the time interval until start of RT
- A high psychological burden due to “untreated” cancer

this pressure.⁹ Some patients may also suffer clinical symptoms from cancer, such as extreme pain from bone metastasis, brain pressure, or difficulty breathing. In such cases immediate care matters.

For patients, delays can also have significant non-medical consequences. A cancer diagnosis is always a frightening experience. Unnecessarily prolonging this period of uncertainty and fear for days or weeks can be profoundly disruptive to patients and their families.¹⁰ In addition, delays can cause patients to incur additional costs, for example travel expenses, and can force them to take additional time off work.

*Local control is defined as the stopping of cancer growth at the point of origin.

“In patients who are admitted for the initiation of oncological care like RT, or who are admitted for cancer-related problems for which radiation is the answer, timely initiation of treatment can reduce the length of hospitalization.”

Lauren E. Henke, MD

Assistant Professor of Radiation Oncology, Washington University School of Medicine

Healthcare providers

For physicians, delays in radiotherapy also have implications as some treatment options, as well as combination treatments, become more difficult. The need to wait for radiotherapy (RT) makes it difficult to implement it in multimodality therapy schemes; the ability to apply RT when needed makes it easier to intertwine it with other treatment modalities such as immunotherapy or surgery. Often decisions about other therapies are not made until radiotherapy has demonstrated its first effects.

For patients suffering from glioblastoma, a particularly aggressive brain cancer, survival is significantly reduced if RT is not initiated within six weeks after complete resection of the tumor.¹¹

One of the most important tools in cancer care today is multimodality tumor boards. Not being able to confidently offer a reliable starting point for radiotherapy treatment, or plan a personalized treatment schedule, can be a major obstacle.

Currently physicians may feel disempowered by being reliant on rigid processes that they cannot change. If they need to prioritize to a patient who needs immediate treatment, this can often be a complex and time-consuming undertaking. In cases where it is not possible to offer patients the immediate treatment they need, these delays can cause long-term psychological stress to physicians.

Healthcare systems

For hospitals and healthcare systems, delays to radiotherapy can also have a negative impact. Reducing these delays can contribute to fewer wasted activities (e.g. administrative processes and manual steps), lower back-office costs, and a more efficient allocation of workforce. Delays can also have collateral consequences; during this time, some patients may be inclined to seek other medical advice or options, leading some to forego treatment to pursue alternative non-radiotherapy treatment or to seek care from a different provider or system. Patient attrition carries a significant financial cost.

Shorter hospital stays also offer important financial advantages. Some patients with advanced cancers or significant comorbidities must be hospitalized during the time they are waiting for treatment. Some of these hospitalized patients may need urgent radiotherapy, such as spinal cord compressions and bleedings. Some will be discharged at the completion of treatment. In some parts of the world such as China, most radiotherapy patients are inpatients. For these patients, reducing time-to-treatment initiation from weeks to days has clear benefits, in financial savings and in freeing up bed capacity for other patients. In palliative settings, earlier access to radiotherapy reduces the duration of hospital stays for patients with cancer.¹²

Finally, outcomes being compromised by unnecessary or avoidable delays could expose hospitals and providers to legal liability, particularly if treatment was not in accordance with established guidelines. Avoiding this risk is clearly advantageous.

What are the causes of delays?

There is little doubt that delays in time-to treatment initiation are clearly unhelpful and often damaging. But the question of what causes these delays—a question that could lead to possible solutions to the problem—is more difficult to answer.

The delays that currently exist can be attributed to a combination of six principal factors:

- Overburdened healthcare systems struggling to deal with increased demand—a problem made even more acute by the anticipated post-Covid surge in cancer cases.¹³
- Shortages of medical staff, including medical physicists and technologists as well as support and administrative staff.
- Limited availability of treatment sites and radiotherapy technology.
- The number of manual steps currently required before radiotherapy treatment can begin. These can include additional imaging to simulate treatment, requiring an extra patient appointment, the contouring of the target tumor and organs at risk, and treatment plan optimization.
- Complexity of modern radiotherapy treatments. For example complex manual treatment planning can take time because of trial and error, searching for the best treatment plan.
- Many cancer patients are receiving a combination of different treatment types, such as immunotherapy and radiotherapy. These different types are delivered by different departments. Because of a lack of treatment planning agility, the non-coordinated treatment schedules of each can result in delays or suboptimal timing for patients.



21%

of cancer patients in the UK who receive an urgent referral for suspected cancer are not seen by a specialist within 2 weeks.²



The solution

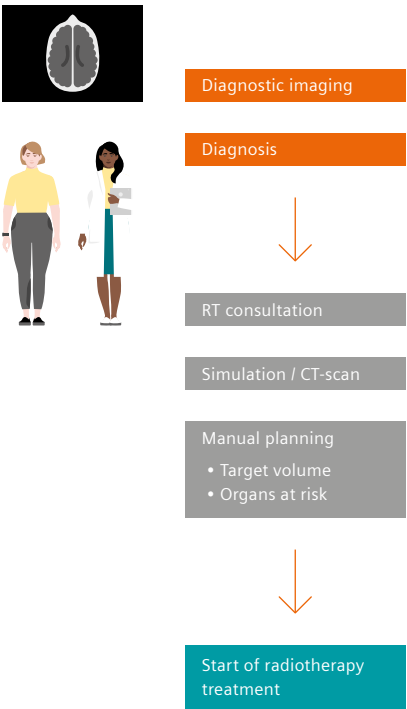
Accelerating the path to radiotherapy treatment and transforming a process that takes weeks into hours requires a combination of workflow re-design and innovative

technology. Through these, greater speed and agility can be achieved, which in turn offers downstream opportunities to improve the way care is delivered.

Starting radiotherapy in hours instead of weeks

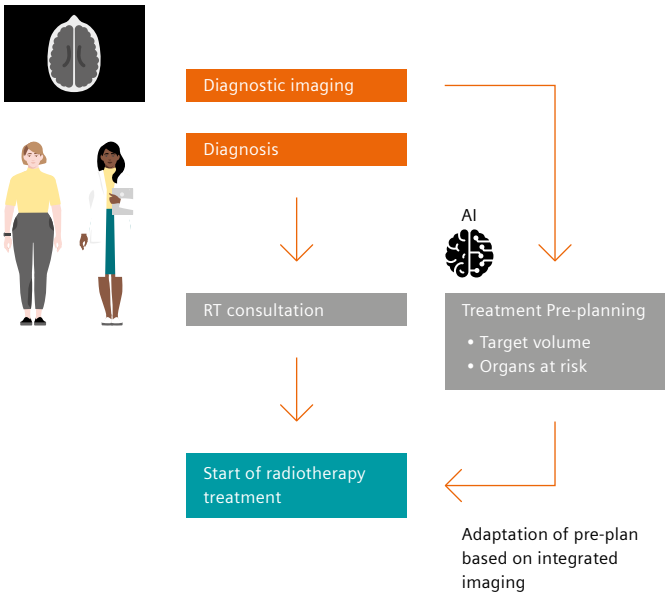
Accelerating the path to treatment to maximize agility and impact

Current radiotherapy treatment pathway



- Diagnosis
- Time to treatment
- Treatment

Accelerated radiotherapy treatment pathway



“The cases today which need treatment urgently do not have access to such care because of technological limitations. If we eliminate the technological limitations, clinical teams will be organized around those tools to treat those patients right away, but all other cases benefit from this speed and agility as well.”

Sasa Mutic, PhD
Senior Vice President, Varian

Changing the treatment planning process

Overall, radiation cancer treatment programs have become shorter and the efficiency of workflows has been enhanced through better planning software, digitalization and automation of individual workflow steps. However, the patient pathway from diagnosis, therapy decision, and treatment planning, to the start of treatment remains a series of separate events. Significant portions of this pathway could be performed in parallel or omitted completely. With today's technologies, it is possible to accelerate treatment planning based on diagnostic images even before the patient comes for consultation. It remains necessary for a radiation oncologist to see the patient. In case of palliation, the physician needs to know the location of the pain. In case of curative treatments, it is also necessary that all imaging is done, including planning a CT-scan, and the clinician must have done the contouring of the tumor before any treatment planning (and automated contouring of organs at risk) can start.

Through new technologies, the task of treatment planning on the day of consultation can be reduced to adapting an already pre-calculated plan to the final treatment position, which can be performed in the treatment room based on integrated imaging.

Shortening time from consultation to treatment



Consultation



Simulation



Treatment planning



Treatment



Time to treatment

From 2 weeks to 2 hours
to start of treatment

“Instead of telling the patient I could bring them down for simulation tomorrow, and start urgent treatment a day or two later, I could just tell the patient that I am going to bring them down for treatment tomorrow.”

Lauren E. Henke, MD

Assistant Professor of Radiation Oncology, Washington University School of Medicine

Technical enablers

To ensure that these parallel processes can be implemented quickly and easily, data completeness and interoperability are key. Manual steps to understand scanning protocols, porting data, or troubleshooting would make it highly inefficient to generate personalized treatment plans in advance.

As a second step, the manual workload for treatment planning needs to be reduced. AI-based, fully automated segmentation of organs at risk can go a long way toward minimizing manual work and ensuring consistent quality of diagnostic data. Today's deep learning-powered technology can automatically identify and segment more than 80 organs, thereby facilitating radiation therapy planning for organs at risk.

As a final step, the quality of imaging systems at the radiation treatment machine is key to be able to skip the simulation scan and to do adaptations directly before treatment. One important performance measure is the scan duration: shorter scan times promote a more efficient workflow and avoid motion artefacts while enabling higher-quality images.

The technology of AI-based online adaptation of treatment plans was originally developed to create the first plan. Nowadays it is also used for plan adaptation on the treatment machine, reducing the time needed for daily online adaptive treatments to as little as 15-20 minutes. Such personalized adapted plans can compensate for changes in tumor size, the location of critical organs, and differences in positioning.

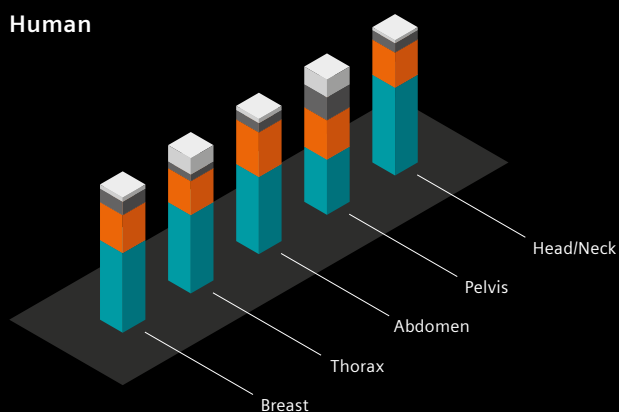
"AI helps us to generate personalized treatment schedules very quickly."

Wilko Verbakel, MD

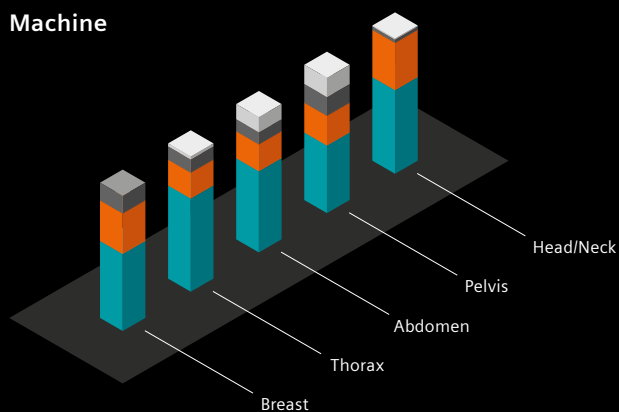
Associate Professor, Senior Medical Physicist, Amsterdam UMC

Increasing efficiency for segmentation of organs at risk in radiation therapy planning supported by AI

Human



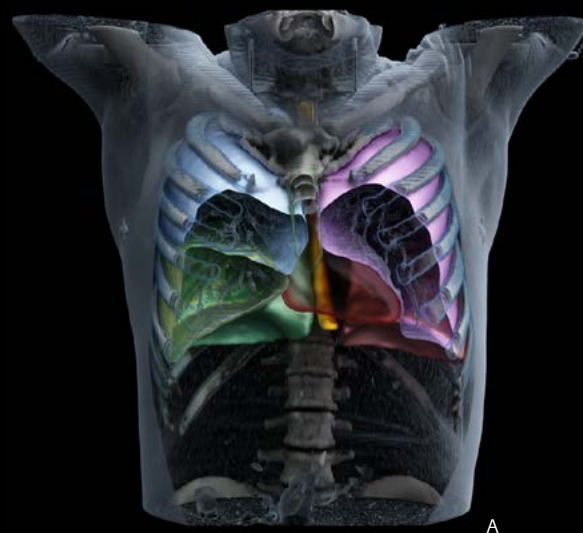
Machine



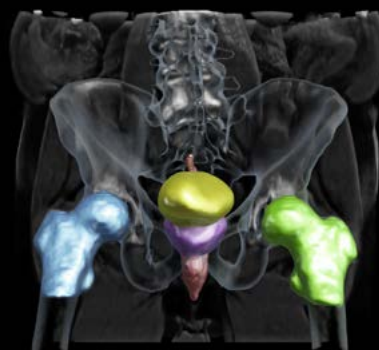
- Usable without editing
- Minor edit needed

- Major edit needed
- Must redo

Organs RT is available on *syngo.via* VB50 and on AI-Rad Companion. | The feedback and the results are from the collaboration performed at UKER. The statements by Siemens Healthineers' customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.



A



B

^A Courtesy of Leopoldina-Krankenhaus Schweinfurt, Germany
^B Courtesy of Aarhus University Hospital, Denmark

“By establishing automated processes, such as auto-segmentation, auto-planning, and streamlined quality assurance, physicians and other staff can free up time from manual work to spend time with patients and on more complex cases.”

Wilko Verbakel, MD

Associate Professor, Senior Medical Physicist, Amsterdam UMC

Benefits

The benefits of a shorter path to radiotherapy treatment are clear. Patients benefit from faster access to care as well as improved quality of treatment plans in comparison with manual plan optimization, improving the likelihood that their treatment will be effective and reducing their stress, clinical symptoms and anxiety. Doctors benefit from greater speed and agility in their treatment delivery options, and being able to treat more patients at the best time for them. Hence overall efficiency is enhanced and more innovative highly precise and personalized cancer treatment delivery methods can be combined and applied more easily. Together with other advances in precision medicine that use patient and tumor data and real-world data analyses, treatment plans can be completely tailored to each individual patient.

Impact of process transformation



Empowered patients



Improved medical outcomes



Reduced costs



Increased number of patients treated

“Automated planning helps us to accelerate the path to treatment and to avoid patient delays.”

Wilko Verbakel, MD

Associate Professor, Senior Medical Physicist, Amsterdam UMC

Case study: Amsterdam UMC

At Amsterdam UMC, a team under the leadership of Dr. Wilko Verbakel, MD, a senior medical physicist, has been the first in the world to develop and implement a “fast-lane” FAST METS protocol and bring it to patients. FAST METS refers to fast metastatic treatment for patients with single bone metastases in the spinal region. The success of this project demonstrates the feasibility of delivering treatments within two hours.

Dr. Verbakel’s team achieved this by flexibly combining a number of innovative solutions. They are the first key benefits along the cancer care pathway with this set-up, allowing them to help palliative cancer patients who in the past would have been forced to come specifically for a CT simulation scan. This step has now been made redundant. Furthermore, the challenges associated with achieving patient positioning similar to the positioning during the CT-scan are eliminated, allowing patients to rest comfortably on a softer mattress.

The key innovation of Dr. Verbakel’s approach is the elimination of the CT simulation of scan for this particular patient group. Under the current pathway, such a scan is a necessary step before the manual process of developing a treatment plan can begin. Under the accelerated pathway, the diagnostic CT images that were acquired earlier for the purpose of diagnosis now go directly into the planning process. This allows radiotherapy to begin earlier.

Proceeding in this way makes it possible to develop a pre-plan that can be adapted later during the treatment session. The first consultation in the FAST METS is done by telephone so that the clinician is sure about the location of the pain. Through the integrated imaging system at the machine there is no need to position the patient exactly the same as during the previously performed CT-scan. When a patient arrives in the treatment room, he/she only needs to lie on the patient table. Based on these images, the pre-plan can be adapted towards a personalized treatment plan for the day. The online adaptive pathway automates most of the process. By adopting this streamlined workflow, patients receive their treatment within two hours after arriving in the hospital. Immediate treatment delivery can be enormously impactful as these patients are often suffering pain from the metastasis.

Looking ahead, it is possible to imagine the extension of FAST METS with expanded digitalization and automation to other patient groups where faster access to treatment has direct impact on survival chances, such as patient groups with oligometastatic tumors and primary head/neck tumors. Oligometastatic tumors include patients with a few well defined metastatic spots—an intermediate stage between a well-defined tumor and metastatic tumors through the entire body. In the future, automation for patients suffering from head and neck cancer can be

particularly impactful as the contouring for head and neck can take up to two hours.

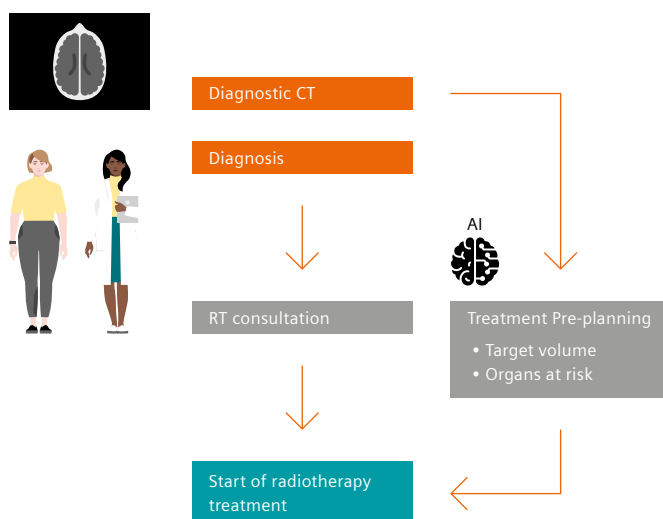
This accelerated path to radiotherapy treatment is most relevant for all patients with clinical symptoms and indications for radiotherapy; for patients with highly aggressive tumors, with a risk of progression in the time interval until start of radiotherapy; and for those patients with a high psychological burden due to “untreated” cancer.

FAST METS initiative Amsterdam UMC, Cancer Center Amsterdam

Starting Radiotherapy in hours instead of weeks

- Diagnosis
- Time to treatment
- Treatment

Accelerated radiotherapy treatment pathway



Requirements:

- **Imaging:** Diagnostic CT
- **Stand-by team:** Attending radiation oncologist, treatment planners and medical physics, radiotherapy technologists
- **Technology:** high quality integrated imaging and adaptive treatment planning



Current timeline for same day treatment in Amsterdam UMC (for known metastatic cancer patients)

10:00	RT consultation
10:10	Adapt pre-plan to treatment machine
10:30	Approve adapted plan by physician and physicist
10:35	Scan patient with integrated CT and adapt plan
10:40	Start treatment

Leadership strategies

The approach taken by Dr. Verbakel in Amsterdam, as well as the general approach discussed in this paper, offer a series of strategies that can be applied throughout many parts of today's healthcare system. These include the following:

Generate a positive mindset about AI and digitalization

Today, many physicians and technologists view AI and digitalization as a threat to replace their work. Healthcare leaders must effectively communicate that AI and digitalization are not just about "technology" but about practical tools that can make life easier for a broad range of healthcare workers, removing burdensome and repetitive parts of their work to free up time for other more important tasks such as more human interaction, dealing with more complex cases, and treating more patients.

Manage expectations based on rigorous patient stratification

Rigorous and realistic patient stratification is important to speed up the adoption of this accelerated path to treatment in clinical practice. Decisions about which patients are eligible for which type of treatment, and which patients would benefit most and need fastest access to treatment can provide valuable guidance on how to make process decisions. Taking patient eligibility into account is important; otherwise physicians might find themselves under too much pressure to analyze complex cases within an insufficient timeframe, which may result in errors and frustration hindering further adoption.

Seek opportunities to change the cancer care journey

Having the know-how about redesigning workflows and innovative technologies does not mean the transformation will happen on its own. The example discussed in this paper is illustrative. Today many physicians still believe it is not appropriate to treat patients with metastatic disease at the end of their lives for pain relief or prolonging life. Adaptations like this can take years or decades.

Actively redistribute resources

In the future, it is highly likely that we will be able to detect cancer even earlier. A redistribution of cancer cases towards lower stages and an opportunity for more standardized care is anticipated. While this will free up physician time to enhance care for more complex cases, it may also result in a higher case load at each individual treatment unit.¹⁴ While the gained agility and speed described in this paper will help to make radiation therapy more readily available, this may also result in a need for additional treatment units to effectively deal with greater demand. Managing resources actively will be important to avoid frustration and failure in adoption.

Look for growth opportunities

One of the biggest growth opportunities for healthcare systems in oncology is the provision of care in lower resource settings. Easing the need for highly specialized personnel in standardized care settings and combining automation with digitally enabled services such as telehealth or remote treatment planning will enable expanding cancer care to areas where lack of expertise is the bottleneck to care provision today.

The path forward

"In the future more patients are receiving multiple types and courses of therapy, including newer combinations, like immunotherapy and radiotherapy."

Lauren E. Henke, MD

Assistant Professor of Radiation Oncology,
Washington University School of Medicine

This paper illustrates that by smartly combining process and technology innovation it is possible to reduce the path to radiation treatment from weeks to hours. It also shows how transforming one rigid sequence of multiple process steps into one interconnected, adaptive process has the potential to significantly change the course of precision cancer care.

While radiation therapy is already one of the major elements of cancer treatment, greater agility can make it possible for radiation therapy to be utilized more extensively, and to play a bigger part within combination treatments.

Precision medicine is an evidence-based approach that enables treatment decisions and implementation based only on medical considerations and patient preference. Moving towards the described data-driven approach helps to achieve this. At the same time, it prepares the field for what is to come: an avalanche of data that radiotherapy will only be able to capitalize on if technology and processes are in place to incorporate multiple kinds of data.

Today, planning radiotherapy treatment based on multi-modality imaging, such as MRI and PET-CT is becoming increasingly common. Treatment response not only to radiation therapy but also to combination treatments is taken into account. The combination of novel drugs with radiotherapy has the potential to further improve patient outcomes. As a clinical research priority, new drug-



Towards a future with greater agility in radiotherapy

Precision medicine prepares the field for what's to come: an avalanche of data that radiotherapy will only be able to capitalize on if technology and processes are in place.

radiotherapy combinations may be as important as new drug-drug combinations.¹⁵ This will add complexity to monitoring treatment response.

Future workflows will have to be able to take in multiple types of complex data. But it does not stop there. Organ-specific risk stratification based on genomic data has shown promise, as has real-world data collected from previous patients. All these are drivers towards a more agile, data-driven, and impactful utilization of radiation therapy.



Suggested follow-up on

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Wilko is a senior medical physicist and associate professor at Amsterdam UMC in the Netherlands. He is a graduate of the Eindhoven University of Technology with Master degrees in Technical Physics and Design of Physics Instrumentation. After working as a nuclear physicist, he completed his PhD on Boron Neutron Capture Therapy and worked as a medical physicist at VU university medical center in Amsterdam. In addition to clinical work, his research covers a wide range of topics in technical radiotherapy. He has written over 100 scientific peer-reviewed papers and is a board member of the scientific committee of the Dutch Radiation Oncology Society.



Sasa Mutic, PhD
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Varian

Sasa Mutic joined Varian in June of 2020, as the SVP for Radiation Treatment Solutions. In this role, he leads Varian's product development, management, and marketing for linear accelerators, brachytherapy, quality assurance, and treatment planning and treatment management software. Prior to joining Varian he was an Endowed Professor and Vice Chair of Radiation Oncology at Washington University School of Medicine in St. Louis, where he was for 24 years. Sasa is Fellow of the American Association of Physicists in Medicine and is certified by the American Board of Radiology in Therapeutic Medical Physics.



Susanne Baars
Sr. Global Thought Leadership manager
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Siemens Healthineers

Susanne is driven by improving patients' lives worldwide. She does this through her radiant energy, extensive knowledge, and real-world experience working alongside physicians and patients who lack access to care and a global network. She has served in numerous roles in science, government, hospitals, and industry. Inspired by helping patients worldwide, she founded SocialGenomics and the Human Genome Foundation, aiming to integrate access to life-saving information and build multi-stakeholder collaborations in complex environments. She holds Master degrees in Neuroscience & Cognition and Applied Ethics from Utrecht University and co-authored multiple publications. Furthermore, Susanne serves on the Dutch National Health Institute Board of Advisors.



Reto Merges
Global Head Expanding Precision Medicine,
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With more than 10 years' leadership experience in healthcare marketing, Reto Merges has a strong track record in building effective teams for clinical and innovation marketing. In addition, he has four years of work experience in China, ramping up efforts for research collaborations in China and South Korea. He holds a degree in electrical engineering and information technology from the Karlsruhe Institute of Technology, Germany, and has studied at the Nanjing Normal University, China. His scientific background is in the field of medical imaging, where he has authored many publications and holds multiple patents.

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