THERAPANACEA

ART-PLAN™ AdaptBox

White paper | 2024

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Offline adaptive radiotherapy (ART) is emerging in radiation oncology, offering the prospect of enhancing cancer treatment precision.

This approach involves adjusting treatment plans based on analyzed imaging data collected prior to each session, allowing for treatment adaptations to changes in tumor size, location, and overall patient anatomy. By accounting for day-to-day variations, offline adaptive radiotherapy holds the promise of optimizing radiation doses and minimizing harm to surrounding healthy tissues, leading to improved therapeutic outcomes for patients and potentially transforming the landscape of cancer treatment.

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01

Which products offer the same functionalities as AdaptBox?

There were several commercially available products and systems for adaptive radiotherapy. Existing solutions can be categorized into vendor/hardware-specific and software-based.

In terms of integrated software/ hardware approaches:

- **Varian/Siemens Healthineers,** a leading company in radiation oncology, offers a range of adaptive radiotherapy solutions, including RapidPlan™ for plan optimization and Ethos™ for real-time adaptive treatment delivery.
- **Accuray's tomotherapy systems** suite combines image-guided radiation therapy (IGRT) and intensity-modulated radiation therapy (IMRT) for precise and adaptive treatments.
- **Elekta's Unity™ system** combines high-field magnetic resonance imaging (MRI) with radiation therapy, enabling online adaptive radiotherapy by visualizing tumors and surrounding tissues during treatment.
- **Viewray's MRdian solution** offers advanced online adaptive treatment capabilities using a low field magnetic resonance embedded imaging sensor (0.35T). It encompasses real-time tracking with online replanning capabilities.

In terms of software-based solutions:

- **RayStation™,** developed by RaySearch Laboratories, is a treatment planning system that includes adaptive planning capabilities for improved treatment delivery based on patient-specific changes.

Dedicated integrated hardware/ software solutions are often endowed with online treatment replanning capabilities that isn't the case for vendor agnostic software driven off-line adaptive radiotherapy monitoring and replanning.

02

What are the different components to secure the effective implementation of an adaptive radiotherapy monitoring and planning workflow?

Effective implementation of an adaptive radiotherapy decision support system requires:

Imaging Acquisition: During the treatment course, periodic or daily imaging is performed to monitor anatomical changes in the tumor and surrounding areas.

Daily dose simulation involves calculating and visualizing the distribution of radiation dose that a patient will receive for online Adaptive Radiotherapy (ART), or has received for offline ART during treatment based on the delivered plan and the daily anatomy.

Dose Accumulation: The accumulated radiation dose is calculated, considering the treatment plan changes and the doses delivered during previous sessions.

Decision Criteria: Establishing clear decision criteria for plan adaptation is essential. These criteria should define specific triggers for when and how to modify the treatment plan based on observed changes in the patient's anatomy or dose distribution.

03

What are the main challenges behind the effective implementation of adaptive radiotherapy?

The effective implementation of adaptive radiotherapy presents several challenges that need to be addressed for a successful integration into clinical practice. Some of the main challenges include:

Imaging Quality and Frequency: Adaptive radiotherapy relies on high-quality and frequent imaging to monitor anatomical changes. However, obtaining and processing these images can be time-consuming and may add to the overall treatment time.

Increased Workload: Adaptive radiotherapy can lead to an increased workload for the clinical team due to the need for additional imaging, contouring, and plan adaptations. Balancing this workload while maintaining treatment efficiency can be challenging.

Computational Complexity: The calculation and optimization of adaptive treatment plans involve complex algorithms and increased computational demands. Ensuring efficient and timely plan adaptation can be challenging, especially for resource-limited facilities.

Patient Selection: Identifying suitable patients who will benefit from adaptive radiotherapy can be challenging. Not all cases may necessitate adaptive strategies, and proper patient selection is essential to optimize resources and outcomes.

AdaptBox provides several benefits for the users

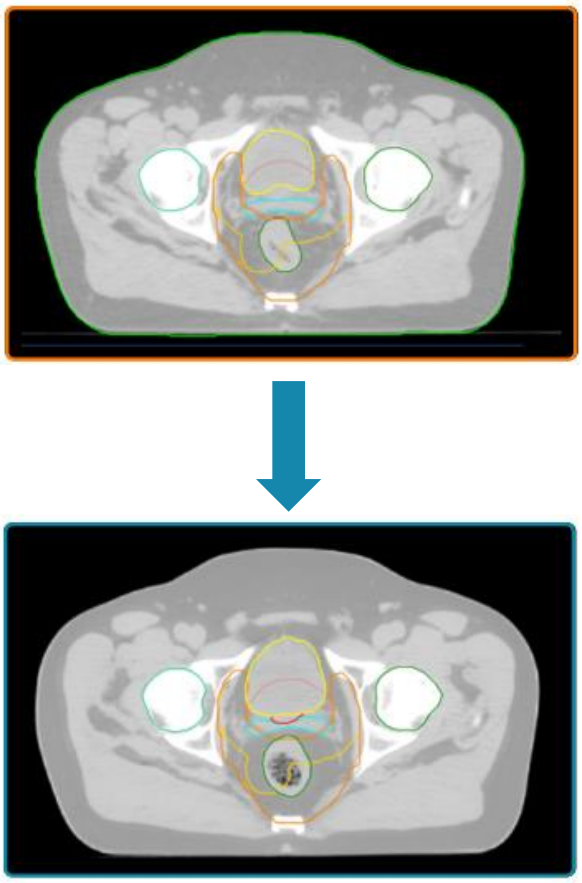
04 (1/2)

How does AdaptBox address these challenges and what is the added value brought from it?

AdaptBox comprises four AI-powered products of ART-Plan™, our proprietary radiotherapy planning solution:

CBCT box addresses the challenge of image quality. It converts Cone Beam Computed Tomography (CBCT) images to planning CT quality. CBCT images may lack the resolution and contrast needed for treatment planning. Converting CBCT to CT quality can enhance image detail and accuracy, enabling better visualization of anatomical structures and potential abnormalities. This led to the generation of a **synthetic CT from CBCT** on which we could implement: (i) more **precise patient positioning** during treatment, (ii) **dose calculation** with respect to the daily delivery plan, and (iii) **automatic annotation of organs at risk**.

Annotate is a **state-of-the-art** commercial solution CE marked and FDA cleared to address the problem of automatic annotation of organs at risk in radiotherapy for **CT and MR imaging.** Annotate relies on the use of a three-layer deep neural network artificial intelligence technique to identify and label critical structures in medical images that may be susceptible to radiation during treatment. Automating the annotation process saves time and reduces inter-observer variability, leading to more precise and efficient treatment delivery.



04 (2/2)

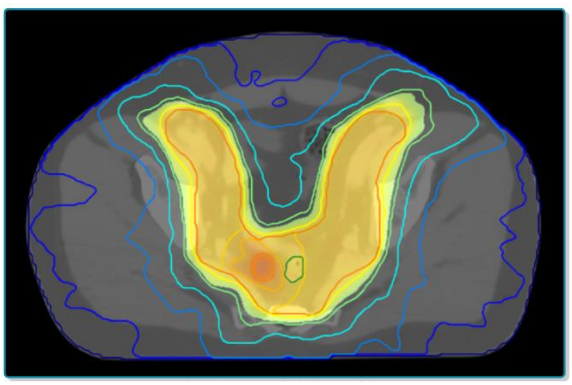
How does AdaptBox address these challenges and what is the added value brought from it?

SmartFuse addresses the challenge of a limited field of view during treatment implementation through **linear and deformable registration.** It augments the **synthetic CT from CBCT** images with the Planning CT (pCT) through registration/fusion between the two signals. This allows to **monitor/compare organ anatomical changes** throughout treatment thanks to contour propagation and **exact dose evaluation and verification** using the daily CBCT images, ensuring that the treatment plan is accurately delivered throughout the treatment course. It could be used to effectively perform dose accumulation either at the organ or at the voxel level.

The Dose management tool addresses the need for fast simulation and is essential to significantly reduce the time required for treatment verification and planning adaptation. Traditional dose calculation algorithms can be computationally intensive and time-consuming. **Deep learning accelerated Collapse Cone** Calculation allows fast dose simulation without compromising accuracy.

By rapidly generating dose distributions, radiation oncologists can quickly evaluate interest to pursue ongoing treatment scenarios, optimize plans, and even consider adaptive strategies based on observed changes during the course of treatment.

AdaptBox is a **vendor/ indication agnostic** while **offering automation and standardization of offline adaptive radiotherapy planning.** It allows the user to streamline adaptive decisions through the definition of anatomical and dosimetric constraints and provides a comprehensive, automated workflow for field-of-view augmentation, contouring of organs at risk, complete dose simulation, and precise visualization of treatment dosimetric discrepancies. **AdaptBox** could be used with **any** existing **linear accelerator** and doesn't require dedicated hardware or specific (other than CBCT) imaging capabilities.



05

How does the conversion of CBCT to CT happen?

Our proprietary patent-pending technology uses the latest advances in Generative AI image translation in medical imaging.

It is an advanced technology that holds great promise for advancing healthcare diagnostics and treatment. Leveraging deep learning models, such as Generative Adversarial Networks (GANs) and Variational Autoencoders (VAEs), this innovative approach allows seamless translation of medical images between different modalities or domains. By training on large datasets of paired or unpaired images, the generative AI model could transform images from one modality, like MRI, CT, CBCT, or PET, into another with high accuracy and precision. This transformative capability has the potential to eliminate the need for repeated imaging, reduce patient radiation exposure, and enable cross-modality comparisons for comprehensive diagnoses.

The size of the training set plays a crucial role in the success and generalizability of generative AI image translation in medical imaging. Through our **clinical research partners and installed base**; a comprehensive vendor/indication agnostic cohort composed **of several hundred thousand** pairs of CT-CBCT **3D volumes**, and **several hundred million images** were built.

This unique data set led to:

- **State of the art Model Performance**: Generative AI models, especially those based on deep learning, thrive on large and diverse datasets. A substantial dataset of paired images enables the model to learn complex patterns and correlations across different modalities or domains, leading to improved translation accuracy and fidelity.
- **Generalization and Robustness:** A larger dataset helps the model to generalize better to unseen data. It enhances the model's ability to handle various imaging variations, patient demographics, and clinical scenarios, making it more robust and adaptable in different healthcare settings.
- **Adaptation to New Domains:** A sizable dataset allows the AI model to adapt to new imaging modalities or domains more effectively. This adaptability is crucial in medical imaging, where emerging technologies and techniques continuously expand the range of available imaging data.

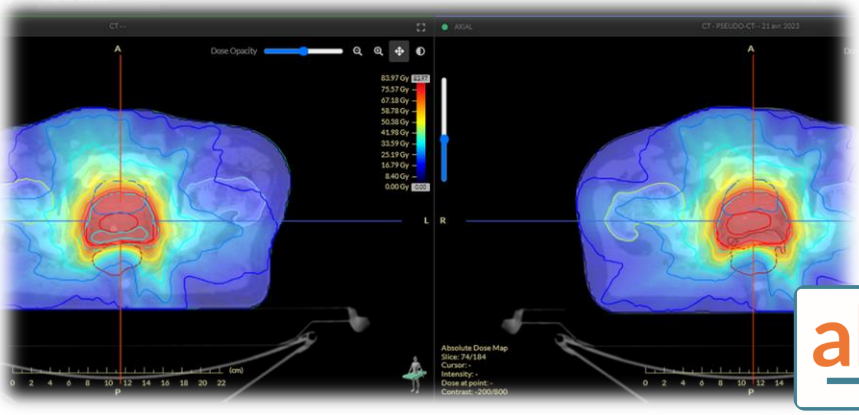
06

Does AdaptBox offer the ability to visualize the intermediate steps of replanning decision-making and provide the user interaction means towards improving its recommendations?

The backbone of AdaptBox, ART-Plan™, has a front/back-end architecture offering numerous advantages. This architecture divides the web application into two main components: the front-end (client-side) and the back-end (server-side).

AdaptBox offers:

- **Seamless User Experience:** By utilizing a front-end web viewer, medical professionals can access and visualize medical images directly from their web browsers without the need for specialized software installations.
- **Interactive Visualization and Monitoring:** Furthermore, users are able to visualize, assess performance, and correct recommendations of the system throughout the different steps of adaptive planning decision making.
- **Scalability and Performance:** The front-end web viewer offloads much of the computational workload to the user's device, enhancing the overall performance and scalability of the system.
- **Collective Assessment:** The front-end web viewer can facilitate real-time collaboration among healthcare professionals. Multiple users can simultaneously view and discuss, enabling quick and effective decision-making.



07

What are the main strengths of AdaptBox compared to its competitive products?

To the best of our knowledge, AdaptBox is the first fully effective , generic, hardware-agnostic, indication-agnostic holistic software-driven adaptive radiotherapy that, once compared to hardware-specific alternatives such as Varian/Siemens Healthineers Ethos™ product, Accuray's TomoTherapy system, & Elekta's Unity™ online adaptive radiotherapy solutions, **offers distinct advantages that are of significant interest in the field of radiation oncology:**

Versatility: Generic software-driven solutions are designed to work across different treatment machines, making them adaptable to various healthcare environments. This versatility allows for broader implementation and usage, irrespective of the equipment vendor.

Interoperability: These solutions are more likely to comply with industry standards, ensuring seamless integration with existing treatment planning systems, Picture Archiving and Communication Systems (PACS).

Flexibility: Generic software-driven adaptive radiotherapy solutions can be updated and improved more rapidly, accommodating new treatment guidelines, technological advancements, and emerging adaptive techniques.

Cost-Effectiveness:
Implementing a generic software-driven approach can reduce costs significantly since it eliminates the need for purchasing specialized hardware for each treatment machine in particularly expensive imaging sensors.

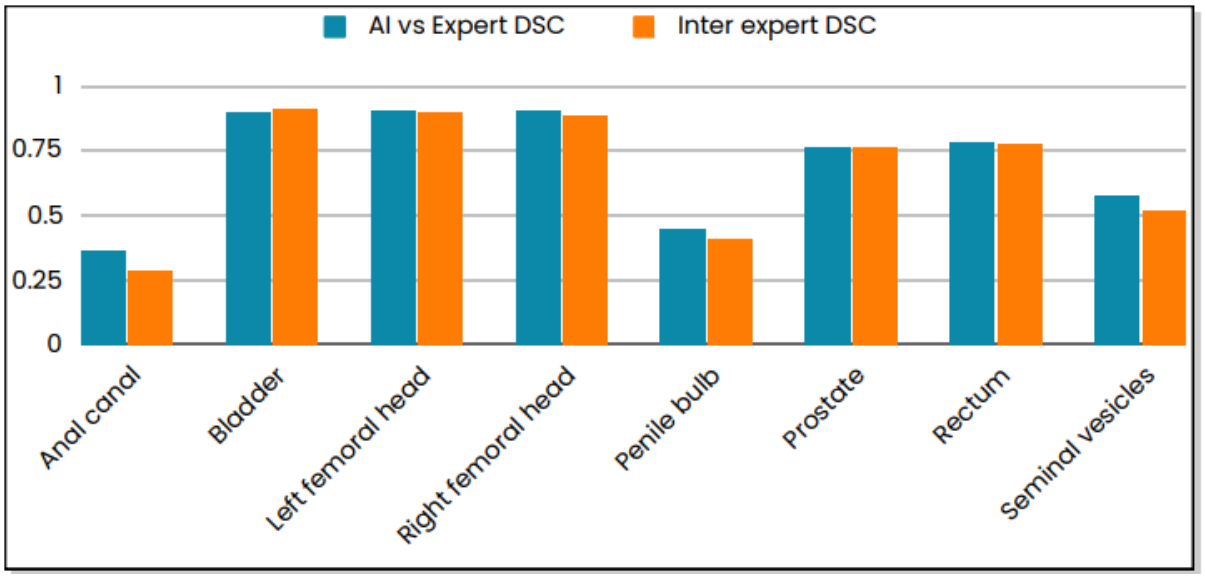
08

How AdaptBox performance was assessed?

AdaptBox, a cutting-edge medical device, holds a prestigious Class II.b classification in compliance with the latest European Medical Device Regulation (MDR).

Its rigorous evaluation followed a meticulous approach, encompassing both individual assessments for each component and a comprehensive analysis of the overall risk associated with the product's usage. The evaluation process entailed real dose measurements, ensuring precise and high-quality performance of the Dose management tool.

Additionally, expert annotations were utilized to assess the exceptional capabilities of Annotate, while the validation of SmartFuse's proficiency was done through qualitative evaluation of the fusions by clinical experts. Further insights and comprehensive details can be found in the white papers of the individual products, providing a comprehensive and transparent understanding of AdaptBox's groundbreaking features and unparalleled performance.



Overall results of Annotate DSC vs inter-expert DSC per organ

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