

# **RefleXion® X1 with SCINTIX® biology-guided radiotherapy**

## **Category:**

Best Medical Technology

## **Company Name:**

RefleXion Medical

## **Product/Solution Name:**

RefleXion® X1 with SCINTIX® biology-guided radiotherapy

## **Compound/Tech Name:**

SCINTIX biology-guided radiotherapy

## **Trade Name:**

SCINTIX

## **Corporate Name:**

RefleXion Medical, Inc.

## **Date of Approval:**

2023-02-01

## **Indications:**

The RefleXion X1 machine with SCINTIX biology-guided radiotherapy is indicated for FDG-guided treatment, which includes modeling, planning, and precise delivery of FDG-guided radiation therapy, a type of Biology-guided Radiotherapy (BgRT) in five or fewer fractions for adults. It is indicated for tumor volumes in lung and bone subject to potential motion and positional uncertainty that have each been assessed with on-board PET/CT prior to delivery for adequate localization, sufficient FDG metabolic activity, local contrast and consistent biodistribution to meet the RMRS requirements, while minimizing the delivery of radiation to vital healthy tissue. BgRT involves the detection of signals from F18 during active beam delivery as a guide to deliver megavoltage X-ray radiotherapy in a rotational, modulated format in accordance with a physician approved treatment plan.

The RefleXion X1 system is also indicated for treatment planning and precise delivery of image-guided radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery for tumors or other targeted tissues anywhere in the body when radiation treatment is indicated while minimizing the delivery of radiation to vital, healthy tissue. The megavoltage X-ray radiation is delivered in a rotational, modulated, image-guided format in accordance with the physician approved plan.

## **Therapeutic Areas:**

RefleXion's SCINTIX Biology-guided Radiotherapy (BgRT) is currently FDA-cleared for the treatment of tumors in the lung or bone arising from primary or metastatic cancer. Currently, RefleXion is conducting comprehensive clinical trial programs to expand the FDA-cleared indications of SCINTIX therapy within the oncology space to include other anatomical locations (e.g., for liver and abdominal cancers, with results expected in mid-2025). Long term, RefleXion's goal is to offer its SCINTIX therapy for the treatment of any solid tumor type of any stage.

The best treatment plan for many patients with metastatic disease combines multiple therapies, with SCINTIX being best suited to reduce or even ablate the bulky disease compartment, while systemic therapies would target micrometastatic disease. When added to chemotherapy, immunotherapy, or targeted drugs, SCINTIX therapy may improve outcomes for patients with lung and bone tumors of any stage and may become the standard of care in many disease situations.

## **General Information File Document upload:**

**[2020 Shirvani Biologyguided radiotherapy redefining the role of radiotherapy in metastatic cancer 1.pdf](#)**

**[RefleXion Announces FDA Clearance for SCINTIX biology guided radiotherapy FINAL R2.pdf](#)**

**[RefleXion Announces Breakthrough Device Designation FINAL.pdf](#)**

**[RefleXion Receives FDA Clearance FINAL.pdf](#)**

**[RefleXion Announces FDA Clearance for SCINTIX biology guided radiotherapy FINAL R2.pdf](#)**

## **Background information and need for drug / device:**

The RefleXion X1 device delivering SCINTIX biology-guided radiotherapy represents a significant advancement in cancer treatment. It uses a radiotracer that interacts with cancer cells, causing them to emit signals. These signals act as real-time beacons, allowing the X1 machine's advanced PET capabilities to precisely target and deliver external-beam radiotherapy to one or multiple tumors simultaneously, all within the same treatment session, even when tumors are moving. By using the tumor's own emissions to guide the delivery of the radiation dose, treatment margins, and the

subsequent radiation dose to healthy tissue may be reduced.

Current challenges in the field of external-beam radiotherapy include tumor motion, limited visualization, and multiple lesions in patients with metastatic disease. Many tumors, especially tumors in the lungs, move with respiration and other bodily functions, making accurate targeting and dosing a challenge. Current technologies often require breath-holding or gating techniques, which generally lead to imprecise delivery of the prescribed external-beam radiotherapy dose and also can cause discomfort to patients. In addition, traditional therapy relies on anatomical imaging to develop a treatment map. This treatment map may not always reflect the accurate biological activity or location of a tumor, which can lead to over or under-treatment. Patients with multiple tumors typically require complex treatment plans and may require increased radiation treatments, or they may not benefit from definitive treatment and are instead offered palliative care.

SCINTIX therapy utilizes PET radiopharmaceuticals that bind to cancer cells, allowing the X1 with SCINTIX to track tumor motion in real time and send beamlets of radiation to destroy them. This ensures precise targeting and delivery, even for moving tumors, while minimizing damage to healthy tissue. By reducing the impact of tumor motion, SCINTIX therapy provides more precise targeting while streamlining treatment plans for patients with one or multiple tumors. In addition, the new radiotherapy approach personalizes treatment by tailoring dose delivery based on the unique biology of each patient's tumor(s), and it may potentially offer treatment for those who were previously not candidates for radiation treatment due to late-stage disease.

By addressing these critical, unmet needs, SCINTIX therapy offers a promising new paradigm in cancer care, with the potential to improve outcomes and quality of life for patients and their family members.

## **Background File Document upload:**

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**[Founders Story FINAL 62524.pdf](#)**

**[230201 SCINTIX Biologyguided Radiotherapy Background FINAL 2.pdf](#)**

## **History of the development of the solution/product:**

External-beam radiotherapy is a main pillar of cancer treatment because it's safe, cost-effective and efficacious, but it has been a complex procedure since first use 100+ years ago. RefleXion's technology is the first self-driving radiotherapy where cancer autonomously directs its own treatment. This 15-year project involved conceptual, electromechanical, and high-energy physics breakthroughs to realize its ultimate translation into clinical use.

Radiotherapy delivers high-energy X-rays to treat cancer. Delivering multiple beams from different points concentrates the radiation dose on the target while minimizing dose to healthy tissue. Tumors move continuously due to biological processes, and overall tumor locations can shift from treatment day to treatment day. As radiotherapy has become more precise, millimeters of motion can cause underdosing or overdosing of nearby structures. Current technologies use sophisticated imaging techniques to compensate for motion uncertainty. These involve a manual process. The complexity increases exponentially as tumor numbers increase. This limits radiotherapy to treating early-stage cancer (1-2 tumors). When cancer spreads to multiple locations (metastatic), conventional external-beam radiotherapy is no longer a curative treatment option.

RefleXion's technology is the first to use PET to close the feedback loop between cancer detection and immediate treatment. RefleXion's innovation combines PET and radiotherapy and harnesses the tumor signals in real time to direct radiation to one or more tumors, even while moving. Because this is an autonomous process, its complexity doesn't increase with the number of targets, which places metastatic disease within reach of potentially curative radiotherapy.

RefleXion's theranostic approach is protected by 250+ patents and patent applications. It required over a decade of development in three areas of fundamental innovation.

1. Rotate a linear accelerator (LINAC) at 60 RPM (60 times faster than conventional devices) around the patient. This had never been done and was further complicated by sensitivity of LINAC's to mechanical forces.
2. Enable PET detection in the presence of the LINAC. The PET system needs to detect radiation signals that are much fainter than the intense radiation delivered by the LINAC. This is akin to trying to see starlight (radiopharmaceutical emissions) when the sun (LINAC) is shining on a bright day. Our patented design selectively "listens" at the right time for these signals so cancer is detected even while it is being treated.
3. Shape the X-ray beam in an order of magnitude faster than other radiotherapy systems due to the fast 60 RPM rotation. A new multi-leaf collimator that could transition heavy tungsten leaves 100 times/second to shape the beam in real time was needed. No technology existed, so we prototyped four different topologies, combining two into a fifth design, resulting in the patented pneumatic-spring-resonance design in use today.

These advances in medical device hardware are embedded in a software ecosystem for treatment planning and treatment delivery that RefleXion built from the ground up.

Stanford treated the first patient with SCINTIX therapy in August 2023, the first time in

history a tumor “self-drove” its own treatment. To date, our technology is in clinical use at seven institutions in the US.

## **Development File Document upload:**

### **ESTRO 2024**

**AbstractStanfordMuratLucasFirstPatientSubmittedOct252023.pdf**

**Full Manuscript BioGuide X study Vitzthum2024BIOGUIDEX A**

**firstinhuman study of the performance of positron emission tomographyguided radiation therapy 1.pdf**

**RefleXion X1 with SCINTIX BgRT.png**

**2020 Shirvani Biologyguided radiotherapy redefining the role of radiotherapy in metastatic cancer 1.pdf**

## **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:**

Because the signals emanating from a radiopharmaceutical are fairly weak, PET images used to diagnose and stage cancer require minutes of signal collection to form a full image. This is analogous to photography requiring longer exposure time in low light. Since effective external-beam radiotherapy requires tracking a tumor that moves continuously with breathing and other motion, sub-second latency between detection and treatment is required. Rather than using the full PET image, RefleXion’s fundamental concept leverages the information contained in thousands of emissions and responds to those with a beamlet of radiation. SCINTIX senses emissions and fires radiation back along that same pathway, “reflecting” the radiation back to its source immediately. This solves the decades-old targeting and motion management problems that have prevented using external-beam radiotherapy efficiently for treating metastatic disease.

Accelerated by progress in diagnosing and treating neuroendocrine and prostate cancers, drug discovery and development activities of academic institutions and the bio-pharmaceutical industry often resulted in an increasing number of cancer types now being detectable and treatable by novel radiopharmaceuticals. SCINTIX leverages both diagnostic and therapeutic radiopharmaceuticals in a new way– something no other external-beam radiotherapy company can.

- Diagnostic: We adapt existing diagnostic radiopharmaceuticals as “BioGuides” for SCINTIX therapy in disease-specific applications (for example in prostate cancer with prostate specific membrane antigen (PSMA)-targeted PET radiopharmaceuticals). This creates an entirely new market opportunity for the radiopharmaceutical industry in therapy guidance and provides a new treatment option.
- Therapeutic: SCINTIX works in concert with targeted radionuclide therapeutics (TRT)

in metastatic disease by using the same biological targeting mechanism (e.g., targets uniquely expressed in specific cancers, like PSMA in prostate cancer) as the TRT. While TRT effectively treats micro-metastatic disease, SCINTIX therapy eliminates multiple sites of resistant, bulky disease, potentially boosting the overall effectiveness of TRT.

To increase the reach of SCINTIX for nearly all solid tumors, we are developing a portfolio of PET radiopharmaceuticals that target specific molecular characteristics of different cancers for more precise SCINTIX delivery. We have two prostate cancer programs targeting PSMA with industry-leading pharmaceutical companies, and we acquired rights to develop our own PET radiopharmaceutical for hard-to-treat cancers, including brain, certain breast, bladder, and pancreatic cancers.

SCINTIX therapy is designed to treat all stages of cancer, providing a new treatment for metastatic disease, where it has the most potential to improve the human condition. In the US alone, 600,000+ patients die from metastatic disease annually, and at diagnosis, when metastatic disease is present, the five-year survival rate is 3%-30%. Currently, few treatment options significantly extend survival with a high quality of life for these patients. Increasing evidence demonstrates that combining locally ablative therapy, such as conventional external-beam radiotherapy, with systemic therapies (immunotherapy or targeted therapeutics) can dramatically affect certain cancers. Conventional radiotherapy approaches can scale to reach 1-2 sites of disease. SCINTIX was conceived to advance radiotherapy, enabling the treatment of multiple disease sites to improve patient outcomes and potentially even offer a cure.

### **Innovation File Document upload:**

**Weber et al What is Theranostics JNM 202327.pdf**  
**2021 Filippi Comprehensive metastatic ablation in advanced NSCLC through biologyguided radiotherapy A path forward\_.pdf**  
**Palma Top Ten Lessons From SABR RCTs.pdf**  
**2019 Palma RJ Beyond OMD.pdf**

### **Please provide appropriate references (PubMed, Abstract, Website):**

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### **References File Document upload:**

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