Introduction
Aarhus University Hospital, ranked the best hospital in Denmark for nine consecutive years\(^1\), delivers approximately 62,000 radiation treatments annually, including stereotactic radiotherapy for around 25 patients with tumors in the liver. This patient group represents some of the most challenging cases, where comorbidities, tumor size, or tumor location preclude surgical resection and other ablative technologies. For cases that require highly accurate and precise radiation targeting, clinicians at Aarhus University Hospital use the TrueBeam\textsuperscript{®} radiotherapy system in conjunction with the Calypso\textsuperscript{®} system featuring implanted Soft Tissue (17G) Beacon\textsuperscript{®} transponders. This combination helps to guide patient setup and manage the significant intrafraction motion that is characteristic of targets in the abdomen.

Overcoming the challenges of liver treatment
Aarhus University Hospital sees approximately 300 cases of liver cancer each year. Based on the number, size, and location of tumors, options for treatment include surgical resection, percutaneous chemical ablation and ablation by radiofrequency, high-intensity focused ultrasound, or microwave techniques. When these approaches are contraindicated, stereotactic body radiotherapy (SBRT) is the definitive treatment. “These are the priorities followed by most institutions in the world,” says Morten Hoyer, MD, PhD, department of oncology. “In this way, we end up treating approximately 25 patients with stereotactic radiotherapy. Colorectal metastasis represents the majority of patients that we treat with radiation.”

Liver tumors located close to large blood vessels, where the cooling effect of blood flow reduces the effectiveness of ablation techniques, are often prime candidates for SBRT. This close proximity to critical structures demands accurate delivery of a high radiation dose with a steep gradient and minimal margins around the target. However, the liver poses specific challenges for high-precision targeting.

Imaging of soft tissue is one challenge. “We cannot image the tumor by itself with a cone-beam CT, as we can when we image a lung tumor,” explains Hoyer. “We can only see the whole liver, and this is not accurate when we are speaking of targeted radiation treatment.”

Tumor motion is an additional challenge. “During treatment, the liver exhibits the largest motion of any organ during treatment,” says Hoyer. “In our experience, a liver tumor may move as much as three centimeters due to respiration,” adds Esben Worm, PhD, department of medical physics. In addition to respiratory motion, target drift is a concern. “We see baseline shifts or drifts of up to one centimeter during a single treatment,” says Worm. “For this reason we need a very safe and reliable surrogate for the position of the tumor.”

Seeing and correcting for tumor motion
To provide a reliable surrogate for tumor position, clinicians at Aarhus University Hospital implant Calypso Soft Tissue Beacon transponders and use them to locate the tumor and track its motion for SBRT.
Three transponders implanted around the liver tumor transmit location information about the target to the Calypso real-time tracking system at a rate of 25 Hz. The system locks onto the signal during patient setup and tracks it continuously throughout the treatment.

With Calypso real-time tracking, Aarhus University Hospital is now performing gated liver treatments. “We had not done respiratory gating for liver SBRT until the Calypso system enabled us to track internal motion. The Calypso system offers Aarhus clinicians the advantage of imaging during treatment without ionizing radiation. “Without adding imaging radiation dose, we can follow motion of what’s going on inside the patients,” says Per Poulsen, PhD, Institute of Clinical Medicine. As a result, clinicians are also able to see intrafraction baseline drifts that they were not aware of previously. “During the course of the treatment, we can observe the drifts, pause the treatment, and correct for them by making couch adjustments,” says Poulsen.

An efficient clinical workflow
The Calypso system does not significantly change the clinical workflow for liver SBRT. When the multidisciplinary team of surgical, medical, and radiation oncologists determines that SBRT is the most appropriate treatment, three transponders are implanted around the tumor, guided by sonography, in an outpatient procedure that typically takes 20 minutes. Lars Peter Skovgaard Larsen, MD, department of radiology, who performs the implant procedure, prefers to use the 17G Beacon transponder, which has a 50-percent smaller cross-sectional area than the 14G version. “In our rather limited number of cases, we have seen no complications from either transponder; however, we know from studies that the risk of bleeding is lower with the thinner needle,” says Larsen.

At simulation, a 4D CT scan with contrast is taken of the exhalation phase. “An advantage of using the Calypso system is that we can plan the treatment on this exhale scan, which usually is of good quality,” says Worm. The transponders are defined along with the target and structure contouring, and then transferred to the Calypso system. The SBRT plan usually consists of a minimum of seven fields. “In planning the fields, some care is involved to consider gantry angles and couch motion to avoid collisions with the Calypso cart,” advises Poulsen.

A new Soft Tissue (17G) Beacon transponder, 50 percent smaller
Tumors in the abdominal region can be difficult to visualize with kV imaging due to the significant amount of motion during treatment delivery and similar densities of tumor and surrounding tissues. In addition, interventional radiologists performing percutaneous implants in these regions prefer smaller needle gauges than the 14G version of the Calypso transponder.

To address these challenges, Varian has introduced a new, smaller Soft Tissue (17G) Beacon transponder that can be used for tracking motion of soft-tissue tumors during treatment delivery. This new soft-tissue Beacon has a 50 percent smaller cross-section area than the current 14G version. Clinicians can use the new transponder to localize a tumor with the added benefit of continuous position tracking and low-latency (<100 ms) beam gating. Use of the Soft Tissue Beacon transponder can provide confidence that the prescribed dose is delivered to the planning target volume (PTV). It also enables a reduction in treatment margins resulting in an increased sparing of normal healthy tissue. The Soft Tissue Beacon transponder has been cleared by the U.S. Food and Drug Administration and is CE marked for implantation into soft tissue throughout the body, with the exception of the lung.
At patient setup, a standard cone-beam CT is obtained to compare with the Calypso system as an extra measure of confidence. “We have more experience with cone-beam CT, so we always take a verification scan,” explains Worm. “To date, Calypso and the cone-beam CT have always agreed.”

**Conclusion: A safer, more accurate therapy**

With the Calypso system, clinicians now are able to provide more accurate therapy. “With gated treatments and real-time tracking, we have been able to reduce margins to 7 millimeters from the 10 millimeters we use for non-gated treatment,” says Hoyer. Reducing margins, however, is only part of the story. “Even with the standard 10-millimeter margin, more normal tissue is spared and the treatment is safer, because you can compensate for drift and hit the target more accurately.”

By compensating for respiratory motion and drift, a dose distribution that is much closer to the prescribed dose can be delivered. “We believe real-time tracking with the Calypso system reduces the chance of side effects and may ultimately enable us to increase the dose for improved outcomes,” says Hoyer.  

1 Ranked best hospital in Denmark for the years 2008 through 2016 by Dagens Medicin, an independent newspaper that reports on the healthcare sector.