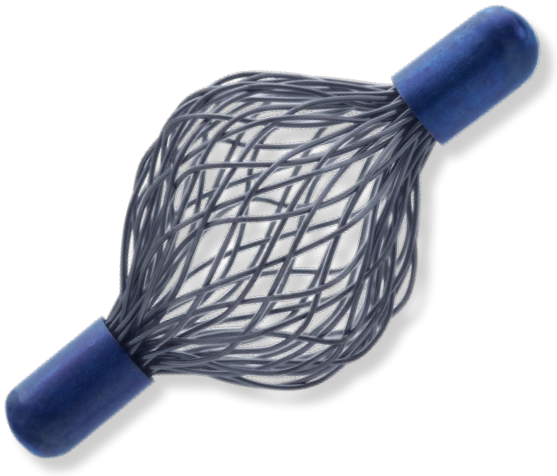


HOLOGIC®
The Science of Sure

Utilizing Site Markers for Long-term Imaging

Exploring the Benefits of Nitinol-based Tumark® Biopsy Site Markers

Nitinol is an innovative alloy that enables clinicians to not only address their breast surgical procedure today but maintain ongoing monitoring of an area into the future. For Hologic's Tumark® Biopsy Site Markers, the material is an essential component to maintaining efficient application and minimal migration. These breast site markers can help clinicians plan their localization procedures, including monitoring regions of interest long-term.

For more information, contact your Hologic representative or visit our website.

https://www.hologic.co.uk/en-gb/products/tumark-securmark-trimark-breast-biopsy-site-markers#230548828-746859052

Tumark®
Biopsy Site Markers

Biopsy site markers are essential to localizing lesions ahead of the procedure—however, not all markers are alike.

Hologic's Tumark Biopsy Site Markers are made with high-quality nitinol, which is a metal alloy composed of nearly equal atomic percentages of nickel and titanium for an implantable device that exhibits superelasticity and shape memory.[1] This is particularly important for the Tumark markers, as it utilizes a smaller application needle and then self-expands to shape, while also offering better tissue anchoring for long-term placement. In an initial data collection study, there was no marker migration when placed under ultrasound, as measured on the post procedure mammogram.[2]

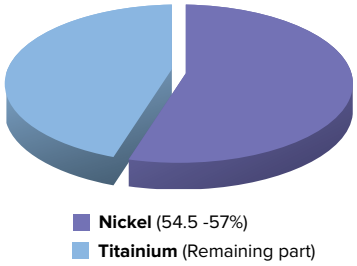
Nitinol is popular for medical devices due to its biocompatibility, superelasticity and fatigue and kink resistance and used in catheter tubes, guidewires, stone retrieval baskets, filters, needles, dental files and archwires and other surgical instruments.[3] These critical characteristics of nitinol—superelasticity and shape memory—are why Hologic utilizes the material for Tumark site markers.

Tumark Marker Composition

Tumark site markers are made from high quality, medical grade nitinol. The alloy conforms to ASTM Designation F2063-18 "Wrought Nickel-Titanium Shape Memory Alloys for Medical Devices and Surgical Implants" and has been tested for biocompatibility in accordance with ISO 10993-1:2018 international standards for implantable medical devices. As a biocompatible implant grade nitinol, the nickel proportion is nominally 54.5% to 57% by weight percent, which reflects a near equal atomic ratio of nickel to titanium.

By utilizing nitinol for the Tumark site markers, Hologic has been able to develop five distinct shapes that are designed to provide visibility in ultrasound and mammography, as well as visibility and compatibility with MRI for operations up to three Tesla. In fact, in 85% of marker placements, physicians stated that the ultrasound visibility was good to excellent upon deployment.[2]

In particular, the largest of the site markers, Tumark® Vision, has high echogenicity in ultrasound due to its three-dimensionality. A 2018 study noted that the dimensionality



of the Vision site marker, "makes the clip marker highly visible from different angles and transducer positions."[4] The study found that is all cases the Tumark Vision marker could be observed on both axes after application when utilizing ultrasound.[2]

In addition to the visibility under ultrasound and mammography, two of the three-dimensional markers have MRI compatible deployment. Just like the radiographically and radiologically uses, markers expand into shapes upon deployment and anchor firmly in the tissue[5] for long-term visibility.

For patients undergoing the less invasive axillary surgical procedure, Targeted Axillary Dissection (TAD), the Tumark Vision marker enables improved long-term visibility when imaged with ultrasound.[6] The Tumark Vision marker was visible in 79.7% of patients who had the marker placed in their axillary lymph nodes as a part of the TAD procedure.[6]

While patients with nickel allergies are contraindicated from using the Tumark site markers due to the nickel portion, there is no reason to believe that this exposure increases the probability of nickel sensitization or exposure to toxins.

> "Since the site markers launched in 1999, over 870,000 have been sold worldwide with no recalls reported."

Biocompatible Material

As previously noted, nitinol is a biocompatible metal alloy, which, in addition to its material characteristics of superelasticity and shape memory, is essential for its successful use as a long-term implant material. Nitinol has shown and proven its eligibility as a medical implant material with long term biological resistance and acceptance, not only for breast site markers but also for cardiovascular implants.[7]

While long-term exposure to nickel can cause an allergy to the alloy to develop over time (sensitization), the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) has established this exposure at the threshold for piercings at 0.2 µg/cm^2/week.[8] In addition to the REACH piercing standards, when looking at the toxicology of nickel based on oral intake, the United States Environmental Protection Agency found that, on average, daily intake of nickel ranges from 100-300 µg/day.[9] In looking at these standards for piercings and oral intake, Hologic's internal laboratory tests on the Tumark biopsy marker determined that the release of nickel was significantly below these thresholds. The largest marker, Tumark Vision, released the most nickel on the first day, and then decreased over the next 72 hours to less than 10 ng per day/cm (0.01 µg/day).[10] Based on this daily data release, the nickel release over the next 60 days can be projected in the chart below.[10] Studies have shown that the release of nickel from nitinol has been seen to decrease even further.[11]

Additionally, the 2018 study of the Tumark Vision marker noted that: "Due to its high chemical stability, nitinol is biocompatible and used in several medical implants such as vascular stents. Laboratory trials show that there is almost no release of material into the tissue. Therefore, it is expected that the marker will remain stable in the tissue for several months, in contrast to some non-metallic clip markers."[2] Nitinol has significant benefits for site markers over other materials, as it can be compressed while remaining intact and smooth. This limits the exposure to nickel as the titanium dioxide coating maintains shape without deterioration.[12]

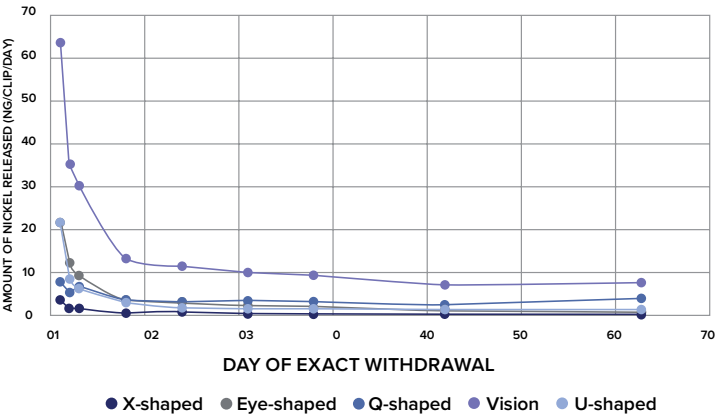
Nitinol is an essential component to the efficient application and minimal migration of these markers. By utilizing these material performance properties, Hologic's Tumark breast site markers help clinicians plan their localization procedures, including helping to observe regions of interest long-term. Since it enables compression into a small canula, the deployment of the biopsy markers is efficient, as it expands within the breast tissue and anchors into place.

These benefits significantly outweigh the concerns of a nickel reaction in patients without an existing allergy, as the Tumark site markers release significantly less nickel post-procedure than even what is consumed by the average individual.

> "Tumark site markers release significantly less nickel post-procedure than even what is consumed by the average individual."

Nitinol is an innovative alloy that enables clinicians to not only address the procedure today but maintain ongoing monitoring of the area in the future.

Course of Actual Nickel Release from Tumark Clips (per clip)



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CE 0482 Tumark® biopsy site markers