Prior Authorization Review Panel  
MCO Policy Submission

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CPB 0886 Optical Coherence Tomography and Microelastography for Solid Tumors and Other Selected Indications

This CPB has been revised to state that the use of optical coherence tomography for margin definition of basal cell carcinoma before Mohs micrographic surgery is considered experimental and investigational.

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<th>Name of Authorized Individual (Please type or print):</th>
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<td>Dr. Bernard Lewin, M.D.</td>
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Optical Coherence Tomography and Microelastography for Solid Tumors and Other Selected Indications

Number: 0886

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers intra-operative optical coherence tomography/microelastography experimental and investigational for the following indications (not an all-inclusive list) because the effectiveness of this approach has not been established:

- Assessment of lymph nodes or tumor margins in breast conserving surgery
- Solid tumor (e.g., breast, gastro-intestinal, glioma, kidney, liver, lung, prostate, and soft
tissue sarcoma) surgery including optical biopsy of lymph nodes, and guidance for real-time determination of surgical margins

Aetna considers intra-operative polarization-sensitive optical coherence tomography experimental and investigational for the following indications (not an all-inclusive list) because the effectiveness of this approach has not been established.

- Assessment of lymph nodes or tumor margins in breast conserving surgery
- Prostatectomy
- Vogt-Koyanagi-Harada (VKH) disease

Aetna considers the use of optical coherence tomography for margin definition of basal cell carcinoma before Mohs micrographic surgery experimental and investigational because the effectiveness of this approach has not been established.

See also
CPB 0269 - Breast Biopsy Procedures
CPB 0383 - Mohs Micrographic Surgery
CPB 0386 - Breast Transillumination, Electrical Impedance Scanning (EIS), and Elastography.

Background

Optical Coherence Tomography:
Diffuse optical tomography is an imaging technique that has been pursued as an alternative to X-ray mammography. While this approach allows non-invasive optical imaging of the breast, it cannot resolve features at the cellular level. Optical coherence tomography (OCT) is a high-resolution, near-infrared (IR) light imaging modality capable of visualizing microscopic features within tissue and is analogous to ultrasound except reflections of near-IR light are detected rather than sound. Optical coherence tomography can perform cellular-level imaging at the expense of imaging depth. The use of intra-operative OCT may shift the microscopic assessment of tissue from post-operative assessment in the pathology laboratory, which offers limited sampling of the margin, to real-time, point-of-care assessment in the operating room, with improved comprehensive sampling of the surgical margin. However, the effectiveness of this approach has not been established.

McLaughlin et al (2010) stated that histologic assessment is the gold standard technique for the identification of metastatic involvement of lymph nodes in malignant disease, but can only be performed ex-vivo and often results in the unnecessary excision of healthy lymph nodes, leading to complications such as lymphedema. Optical coherence tomography has the potential to provide in-vivo assessment of tissue involvement by cancer. In this morphologic study, these researchers showed the capability of OCT to image nodal microarchitecture through an assessment of fresh, unstained ex-vivo lymph node samples. Examples included both benign human axillary lymph nodes and nodes containing metastatic breast carcinoma. Through accurate correlation with the histologic gold standard, OCT is shown to enable differentiation of lymph node tissue from surrounding adipose tissue, reveal nodal
structures such as germinal centers and intra-nodal vessels, and show both diffuse and well circumscribed patterns of metastatic node involvement.

Nguyen et al (2010) noted that during breast-conserving surgeries, axillary lymph nodes draining from the primary tumor site are removed for disease staging. Although a high number of lymph nodes are often resected during sentinel and lymph-node dissections, only a relatively small percentage of nodes are found to be metastatic, a fact that must be weighed against potential complications such as lymphedema. Without a real-time in-vivo or in-situ intra-operative imaging tool to provide a microscopic assessment of the nodes, post-operative paraffin section histopathological analysis currently remains the gold standard in assessing the status of lymph nodes. Optical coherence tomography, a technique previously used to image breast cancer tumor margins intra-operatively in humans and lymph-node microarchitecture in a rat animal model, was being presented for the intra-operative ex-vivo imaging and assessment of axillary lymph nodes. Optical coherence tomography provides real-time microscopic images up to 2 mm beneath the tissue surface in axillary lymph nodes. Normal (n = 13), reactive (n = 1), and metastatic (n = 3) lymph nodes from 17 human patients with breast cancer were imaged intra-operatively with OCT. These preliminary clinical studies have identified scattering changes in the cortex, relative to the capsule, which can be used to differentiate normal from reactive and metastatic nodes. These optical scattering changes are correlated with inflammatory and immunological changes observed in the follicles and germinal centers. The authors concluded that these results suggested that intra-operative OCT has the potential to assess the real-time node status in-situ, without having to physically resect and histologically process specimens to visualize microscopic features.
Zhou et al (2010) stated that three-dimensional (3D) tissue imaging methods are expected to improve surgical management of cancer. In this study, these investigators examined the feasibility of two 3D imaging technologies, OCT and optical coherence microscopy (OCM), to view human breast specimens based on intrinsic optical contrast. Specifically, these researchers imaged 44 ex-vivo breast specimens including 34 benign and 10 malignant lesions with an integrated OCT and OCM system developed in their laboratory. The system enabled 4 um axial resolution (OCT and OCM) with 14 um (OCT) and 2 um (OCM) transverse resolution, respectively. Optical coherence tomography and OCM images were compared with corresponding histologic sections to identify characteristic features from benign and malignant breast lesions at multiple resolution scales. Optical coherence tomography and OCM provided complimentary information about tissue microstructure, demonstrating distinctive patterns for adipose tissue, fibrous stroma, breast lobules and ducts, cysts and microcysts, as well as in-situ and invasive carcinomas. The 3D imaging capability of OCT and OCM provided complementary information to individual two-dimensional (2D) images, allowing tracking features from different levels to identify low contrast structures that were difficult to appreciate from single images alone. The authors concluded that these results lay the foundation for future in-vivo optical evaluation of breast tissues using OCT and OCM, which has the potential to guide core needle biopsies, assess surgical margins and evaluate nodal involvement in breast cancer.

Sullivan et al (2011) noted that the accurate and rapid assessment of tumor margins during breast cancer resection using OCT has the potential to reduce patient risk. However, it is difficult to subjectively distinguish cancer from normal fibro-glandular stromal tissues in
OCT images, and an objective measure is needed. In this initial study, these researchers investigated the potential of a one-dimensional fractal box-counting method for cancer classification in OCT. They computed the fractal dimension, a measure of the self-similarity of an object, along the depth axis of 44 ultrahigh-resolution OCT images of human breast tissues obtained from 4 cancer patients. Correlative histology was employed to identify distinct regions of adipose, stroma, and cancer in the OCT images. They reported that the fractal dimension of stroma is significantly higher than that of cancer (p < 10(-5), t-test). Furthermore, by adjusting the cut-off values of fractal dimension between cancer, stroma, and adipose tissues, sensitivities and specificities of either 82.4 % and 88.9 %, or 88.2 % and 81.5 %, were obtained, respectively, for cancer classification. The authors concluded that the use of fractal analysis with OCT could potentially provide automated identification of tumor margins during breast-sparing surgery.

Kuo et al (2012) stated that advances in optical imaging modalities, such as OCT, enable one to observe tissue microstructure at high resolution and in real time. Currently, core-needle biopsies are guided by external imaging modalities such as ultrasound imaging and x-ray computed tomography (CT) for breast and lung masses, respectively. These image-guided procedures are frequently limited by spatial resolution when using ultrasound imaging, or by temporal resolution (rapid real-time feedback capabilities) when using x-ray CT. One feasible approach is to perform OCT within small gauge needles to optically image tissue microstructure. However, to-date, no system or core-needle device has been developed that incorporates both three-dimensional OCT (3D-OCT) imaging and tissue biopsy within the same needle for true OCT-guided core-needle biopsy. These researchers developed and demonstrated an
Optical Coherence Tomography (OCT) and micro-CT (X-ray) images are automatically segmented using different...
computational approaches, and quantitatively compared to determine the ability of these algorithms to automatically differentiate regions of adipose tissue from tumor. Furthermore, 2D and 3D results were compared. The authors concluded that these correlations, combined with real-time intra-operative OCT, have the potential to identify possible regions of tumor within breast tissue which correlate to tumor regions identified previously on X-ray imaging (mammography or specimen radiography).

John et al (2013) stated that numerous techniques have been developed for localizing lymph nodes before surgical resection and for their histological assessment. Non-destructive high-resolution trans-capsule optical imaging of lymph nodes offers the potential for in-situ assessment of metastatic involvement, potentially during surgical procedures. Three-dimensional OCT was used for imaging and assessing resected popliteal lymph nodes from a pre-clinical rat metastatic tumor model over a 9-day time-course study after tumor induction. The spectral-domain OCT system utilized a center wavelength of 800 nm, provided axial and transverse resolutions of 3 and 12 μm, respectively, and performed imaging at 10,000 axial scans per second. Optical coherence tomography is capable of providing high-resolution label-free images of intact lymph node microstructure based on intrinsic optical scattering properties with penetration depths of approximately 1 to 2 mm. The results demonstrated that OCT is capable of differentiating normal, reactive, and metastatic lymph nodes based on microstructural changes. The optical scattering and structural changes revealed by OCT from day 3 to day 9 after the injection of tumor cells into the lymphatic system correlated with inflammatory and immunological changes observed in the capsule, pre-cortical regions, follicles, and germination centers found during histopathology. The authors reported for the first
time a longitudinal study of 3D trans-capsule OCT imaging of intact lymph nodes demonstrating microstructural changes during metastatic infiltration. These results demonstrated the potential of OCT as a technique for intra-operative, real-time in situ 3D optical biopsy of lymph nodes for the intra-operative staging of cancer. Moreover, they stated that future in-vivo studies will further determine the clinical impact of OCT on reducing the number of normal lymph nodes removed and subsequently reducing the rate of morbid complications associated with lymph node dissections and breast cancer surgeries.

Patel et al (2013) stated that intra-operative delineation of breast cancer is a challenging problem. These researchers used dye-enhanced wide-field polarization imaging for rapid demarcation of en face cancer margins and OCT for cross-sectional evaluation. Ductal carcinoma specimens were stained with methylene blue. Wide-field reflectance images were acquired at 440 and 640 nm. Wide-field fluorescence images were excited at 640 nm and registered between 660 nm and 750 nm. Optical coherence tomography images were acquired using a 1,310-nm swept-source system. The results were validated against histopathology. Both imaging modalities provided diagnostic information on cancer margins. The authors concluded that combined OCT and wide-field polarization imaging showed promise for intra-operative detection of ductal breast carcinoma.

Butler-Henderson et al (2014) noted that approximately 25% of patients undergoing breast conserving therapy for breast cancer will require a 2nd operation to achieve adequate clearance of the margins. A number of techniques for assessing margins intra-operatively have been reported. This systematic review examined current intra-operative methods for assessing margin status. The final pathology status, statistical measures including
accuracy of tumor margin assessment, average time impact on the procedure and 2nd operation rate, were used as criteria for comparison between studies. Although pathological methods, such as frozen section and imprint cytology performed well, they added on average 20 to 30 minutes to operation times. An ultrasound probe allows accurate examination of the margins and delivers results in a timely manner, yet it has a limited role with ductal carcinoma in-situ where calcification is present and in multi-focal cancer. Moreover, the authors stated that further research is needed in other intra-operative margin assessment techniques, such as mammography, radiofrequency spectroscopy and OCT.

An UpToDate review on “Diagnostic evaluation of women with suspected breast cancer” (Esserman and Joe, 2014) does not mention the use of OCT as a management tool.

Furthermore, the National Comprehensive Cancer Network’s clinical practice guideline on “Breast cancer” (Version 3.2014) does not mention the use of OCT as a management tool.

In a multi-center, prospective, blinded study, Zysk and associates (2015) tested the feasibility of using a hand-held optical imaging probe for the intra-operative assessment of final surgical margins during breast-conserving surgery (BCS) and determined the potential impact on patient outcomes. A total of 46 patients with early-stage breast cancer (1 with bilateral disease) undergoing BCS at 2 study sites, the Johns Hopkins Hospital and Anne Arundel Medical Center, were enrolled in this study. During BCS, cavity-shaved margins were obtained and the final margins were examined ex-vivo in the operating room with a probe incorporating OCT hardware and interferometric
synthetic aperture microscopy (ISAM) image processing. Images were interpreted after BCS by 3 physicians blinded to final pathology-reported margin status. Individual and combined interpretations were assessed. Results were compared to conventional post-operative histopathology. A total of 2,191 images were collected and interpreted from 229 shave margin specimens. Of the 8 patients (17%) with positive margins (0 mm), which included invasive and in-situ diseases, the device identified all positive margins in 5 (63%) of them; re-operation could potentially have been avoided in these patients. Among patients with pathologically negative margins (greater than 0 mm), an estimated mean additional tissue volume of 10.7 ml (approximately 1% of overall breast volume) would have been unnecessarily removed due to false positives.

The authors concluded that intra-operative optical imaging of specimen margins with a hand-held probe potentially eliminates the majority of re-operations. These findings need to be validated by well-designed studies.

Nolan and colleagues (2016) stated that evaluation of lymph node (LN) status is an important factor for detecting metastasis and thereby staging breast cancer. Currently utilized clinical techniques involve the surgical disruption and resection of lymphatic structure, whether nodes or axillary contents, for histological examination. While reasonably effective at detection of macro-metastasis, the majority of the resected lymph nodes are histologically negative. Improvements need to be made to better detect micro-metastasis, minimize or eliminate lymphatic disruption complications, and provide immediate and accurate intra-operative feedback for in-vivo cancer staging to better guide surgery. These researchers evaluated the use of OCT for the intra-operative assessment of human LNs for metastatic disease in patients with breast cancer. They assessed the
sensitivity and specificity of double-blinded trained readers who analyzed intra-operative OCT LN images for presence of metastatic disease, using co-registered post-operative histopathology as the gold standard. The results suggested that intra-operative OCT examination of LNs is an appropriate real-time, label-free, non-destructive alternative to frozen-section analysis, potentially offering faster interpretation and results to empower superior intra-operative decision-making. The authors concluded that intra-operative OCT has strong potential to supplement current post-operative histopathology with real-time in-situ assessment of LNs to preserve both non-cancerous nodes and their lymphatic vessels, and thus reduce the associated risks and complications from surgical disruption of lymphoid structures following biopsy.

Breast Cancer:

Yao and colleagues (2017) stated that breast cancer is one of the most common cancers, and is the 3rd leading cause of mortality in women; OCT enables 3D visualization of biological tissue with micrometer level resolution at high speed, and can play an important role in early diagnosis and treatment guidance of breast cancer. In particular, ultra-high resolution (UHR) OCT provides images with better histological correlation. These investigators compared UHR OCT performance with standard OCT in breast cancer imaging qualitatively and quantitatively. Automatic tissue classification algorithms were used to automatically detect invasive ductal carcinoma in ex-vivo human breast tissue. In this study, human breast tissues, including non-neoplastic/normal tissues from breast reduction and tumor samples from mastectomy specimens, were excised from patients at
Columbia University Medical Center. The tissue specimens were imaged by 2 spectral domain OCT systems at different wavelengths: (i) a home-built ultra-high resolution (UHR) OCT system at 800 nm (measured as 2.72 μm axial and 5.52 μm lateral), and (ii) a commercial OCT system at 1,300 nm with standard resolution (measured as 6.5 μm axial and 15 μm lateral), and their imaging performances were analyzed qualitatively. Using regional features derived from OCT images produced by the 2 systems, these researchers developed an automated classification algorithm based on relevance vector machine (RVM) to differentiate hollow-structured adipose tissue against solid tissue. They further developed B-scan based features for RVM to classify invasive ductal carcinoma (IDC) against normal fibrous stroma tissue among OCT datasets produced by the 2 systems. For adipose classification, 32 UHR OCT B-scans from 9 normal specimens, and 28 standard OCT B-scans from 6 normal and 4 IDC specimens were employed. For IDC classification, 152 UHR OCT B-scans from 6 normal and 13 IDC specimens, and 104 standard OCT B-scans from 5 normal and 8 IDC specimens were employed. These investigators demonstrated that UHR OCT images can produce images with better feature delineation compared with images produced by 1,300 nm OCT system. UHR OCT images of a variety of tissue types found in human breast tissue were presented. With a limited number of datasets, these researchers showed that both OCT systems can achieve a good accuracy in identifying adipose tissue. Classification in UHR OCT images achieved higher sensitivity (94 %) and specificity (93 %) of adipose tissue than the
sensitivity (91%) and specificity (76%) in 1,300 nm OCT images. In IDC classification, similarly, these investigators achieved better results with UHR OCT images, featured an overall accuracy of 84%, sensitivity of 89% and specificity of 71% in this preliminary study. The authors concluded that in this study, they provided UHR OCT images of different normal and malignant breast tissue types, and qualitatively and quantitatively studied the texture and optical features from OCT images of human breast tissue at different resolutions. These researchers developed an automated approach to differentiate adipose tissue, fibrous stroma, and IDC within human breast tissues. They stated that their work may open the door toward automatic intra-operative OCT evaluation of early-stage breast cancer.

Gastro-Intestinal Tumor

Li and co-workers (2017) noted that OCT is a real-time, cross-sectional optical imaging technology. It is analogous to ultrasonography (US), except that OCT uses light waves instead of sound waves, and can provide 3D morphological images of living tissues with a micrometer resolution. Through the use of endoscopes, needles, catheters and laparoscopes, OCT has demonstrated tremendous imaging potential in tumor surgery. The current studies suggest that OCT has potential for clinical applications in the following fields of gastro-intestinal (GI) tumor surgery: (i) early tumor detection and diagnosis -- OCT can distinguish differences between polyp tissue, normal tissue and malignant tissue. It could possibly identify pre-malignant lesions or conditions potentially predisposing to malignancy, such as gastric and intestinal
metaplasia, gastritis associated with Helicobacter pylori, and early gastric cancer involving the mucosa or submucosa. In addition, OCT can differentiate between adenomatous polyps and hyperplastic polyps; (ii) optical biopsy of lymph nodes -- As a high-resolution, near-IR imaging modality, OCT is capable of visualizing microscopic features within tissue, distinguishing lymph node tissue from surrounding adipose tissue, revealing nodal structures such as germinal centers and intra-nodal vessels. Consequently, OCT has the ability to show changes in node microarchitecture during metastatic tumor infiltration; and (iii) intra-operative guidance for real-time determination of surgical margins -- In other tumors such as oral squamous cell carcinoma and breast cancer, it has been demonstrated that OCT can be used to rapidly scan large areas of tissue, to guide at the cellular level the surgical resection of neoplastic disease, and to scan tumor margins for the presence of residual disease, tumor foci, and potentially even metastasizing tumor cells. It implies that colorectal neoplasms surgeons can possibly use the laparoscopic OCT to detect the intestinal tumor margin and lymph nodes during operation in the future, so as to determine the appropriate range of bowel resection and lymph node dissection. The authors concluded that at present, there are few reports about the intra-operative application of OCT in the field of GI tumor surgery; thus there is a tremendous opportunity for further research in this field.

Glioma:
Garzon-Muvdi and colleagues (2017) noted that gliomas are central nervous system (CNS) neoplasms that infiltrate the surrounding brain parenchyma, complicating their treatment. Tools that increase extent of resection while preventing neurological deficit are essential to improve prognosis of patients diagnosed with gliomas. Tools such as intra-operative magnetic resonance imaging (MRI), ultrasonography (US) and fluorescence-guided microsurgery have been used in the surgical resection of CNS gliomas with the goal of maximizing extent of resection to improve patient outcomes. In addition, emerging experimental techniques (e.g., OCT and Raman spectroscopy) are promising techniques that may add to the increasing armamentarium used in the surgical resection of CNS gliomas.

**Pancreatic Cancer**

van Manen and co-workers (2017) stated that pancreatic cancer is the 4th leading cause of cancer-related mortality in the U.S. The minority of patients can undergo curative-intended surgical therapy due to progressive disease stage at time of diagnosis. Nonetheless, tumor involvement of surgical margins is observed in up to 70% of resections, being a strong negative prognostic factor. Real-time intra-operative imaging modalities may aid surgeons to obtain tumor-free resection margins. Full-field OCT (FF-OCT) is a promising diagnostic tool using HR white-light interference microscopy without tissue processing. These researchers composed an atlas of FF-OCT images of malignant and benign pancreatic tissue, and examined the accuracy with which the pathologists could distinguish these. A total of 100 FF-OCT images were collected from specimens of 29 patients who underwent pancreatic resection for various indications between 2014 and 2016. One experienced GI pathologist and 1
Optical Coherence Tomography and Microelastography for Solid Tumors and Other Se...

A pathologist in training scored independently the FF-OCT images as malignant or benign blinded to the final pathology conclusion. Results were compared to those obtained with standard hematoxylin and eosin (H&E) slides. Overall, combined test characteristics of both pathologists showed a sensitivity of 72 %, specificity of 74 %, positive predictive value (PPV) of 69 %, negative predictive value (NPV) of 79 % and an overall accuracy of 73 %. In the subset of pancreatic ductal adenocarcinoma patients, 97 % of the FF-OCT images (n = 35) were interpreted as tumor by at least 1 pathologist. Moreover, normal pancreatic tissue was recognized in all cases by at least 1 pathologist. However, atrophy and fibrosis, serous cystadenoma and neuroendocrine tumors were more often wrongly scored, in 63 %, 100 % and 25 %, respectively. The authors concluded that FF-OCT could distinguish normal pancreatic tissue from pathologic pancreatic tissue in both processed as non-processed specimens using architectural features. They stated that the accuracy in pancreatic ductal adenocarcinoma is promising and warrants further evaluation using improved assessment criteria.

Prostate Cancer:

Muller and colleagues (2017) designed and demonstrated a customized tool to generate histologic sections of the prostate that directly correlate with needle-based OCT pullback measurements. A customized tool was created to hold the prostatectomy specimens during OCT measurements and formalin fixation. Using the tool, the prostate could be sliced into slices of 4-mm thickness through the OCT measurement trajectory. In this way, whole-mount pathology slides were produced in exactly the same location as the OCT measurements were performed. Full 3D OCT pullbacks were fused with the histopathology slides using the 3D...
imaging software AMIRA, and images were compared. A radical prostatectomy was performed in a patient (aged 68 years, prostate-specific antigen [PSA]: 6.0 ng/ml) with Gleason score $3 + 4 = 7$ in 2/5 biopsy cores on the left side (15 %) and Gleason score $3 + 4 = 7$ in 1/5 biopsy cores on the right side (5 %). Histopathology after radical prostatectomy showed an anterior located pT2cNx adenocarcinoma (Gleason score $3 + 4 = 7$). Histopathological prostate slides were produced using the customized tool for OCT measurements, fixation, and slicing of the prostate specimens. These slides correlated exactly with the OCT images. Various structures (e.g., Gleason $3 + 4$ prostate cancer, stroma, healthy glands, and cystic atrophy with septae) could be identified both on OCT and on the histopathological prostate slides. The authors concluded that they successfully designed and applied a customized tool to process radical prostatectomy specimens to improve the co-registration of whole mount histology sections to fresh tissue OCT pullback measurements. This technique will be crucial in validating the results of OCT imaging studies with histology and can easily be applied in other solid tissues as well. This will help improve the efficacy of OCT in cancer detection and staging in solid organs. To these researchers’ knowledge, they were the first to describe a 1-to-1 method for full specimen histopathology matching with needle-based OCT in solid tissue. By demonstrating examples of B-scans and identifying structures on OCT that could also be seen on histopathology, these investigators showed that matching is nearly perfect. Besides prostates, the technology can also be applied in other solid tissues (e.g., breast, kidney, liver, and lung). The technology presented was an important step in order to validate a HR imaging technique as OCT. They noted that when OCT has proven to be valid in the ex-vivo setting, the next step will be to validate the technology in-vivo;
future work will focus on a technique to validate OCT in the prostate using this method in a larger group of patients.

Renal Tumor:

Hekman and associates (2017) discussed intra-operative imaging techniques that may help achieve complete tumor resection in nephron-sparing surgery (NSS) of renal tumors. PubMed was searched for English articles on intraoperative imaging during NSS of renal cell carcinoma published after 2005, and a reference search of retrieved articles was performed. Included studies reported about US, fluorescence imaging, augmented reality, OCT, and ex-vivo MRI. The number of patients included in these studies was limited, and randomized controlled trials (RCTs) have not been performed.

Ultrasonography is a well-established technique to assess tumor localization and may be used to evaluate surgical margins of the resected specimen. Fluorescence imaging with indo-cyanine green (ICG) may help differentiate tumor from normal kidney tissue. It is yet unclear whether fluorescence imaging can detect positive surgical margins. Augmented reality is best studied in robotic laparoscopic surgery, and may be useful for tumor localization and resection, if the problem of tissue deformation during surgery can be solved and more results have to be awaited about OCT and ex-vivo MRI. The authors concluded that US is a widely used technique to assist the surgeon in partial nephrectomy nowadays, while the use of fluorescence imaging and augmented reality is emerging. They stated that although various techniques can be used during NSS, the added value of intra-operative imaging to support negative surgical margins remains to be demonstrated.
Soft Tissue Sarcoma:

Mesa and colleagues (2017) noted that sarcomas are rare but highly aggressive tumors, and local recurrence after surgical excision can occur in up to 50% cases. Thus, there is a strong need for accurate tissue differentiation and margin assessment to reduce incomplete resection and local recurrence. These researchers examined the use of OCT and a novel image texture-based processing algorithm to differentiate sarcoma from muscle and adipose tissue. In this study, tumor margin delineation in 19 feline and canine veterinary patients was achieved with intra-operative OCT to help validate tumor resection. While differentiation of lower-scattering adipose tissue from higher-scattering muscle and tumor tissue was relatively straightforward, it was more challenging to distinguish between dense highly scattering muscle and tumor tissue types based on scattering intensity and microstructural features alone. To improve tissue-type differentiation in a more objective and automated manner, 3 descriptive statistical metrics, namely the coefficient of variation (CV), standard deviation (STD), and range, were implemented in a custom algorithm applied to the OCT images. Over 22,800 OCT images were collected intra-operatively from over 38 sites on 19 ex-vivo tissue specimens removed during sarcoma surgeries.

Following the generation of an initial set of OCT images correlated with standard hematoxylin and eosin-stained histopathology, over 760 images were subsequently used for automated analysis. Using texture-based image processing metrics, OCT images of sarcoma, muscle, and adipose tissue were all found to be statistically different from one another (p ≤ 0.001). The authors concluded that these findings demonstrated the potential of using intra-operative OCT, along with an
Optical Coherence Microelastography:

Kennedy et al (2015) stated that an accurate intra-operative identification of malignant tissue is a challenge in the surgical management of breast cancer. Imaging techniques that help address this challenge could contribute to more complete and accurate tumor excision, and thereby help reduce the current high re-excision rates without resorting to the removal of excess healthy tissue. Optical coherence microelastography (OCME) is a 3-D, high-resolution imaging technique that is sensitive to micro-scale variations of the mechanical properties of tissue. As the tumor modifies the mechanical properties of breast tissue, OCME has the potential to identify, on the micro-scale, involved regions of fresh, unstained tissue. Optical coherence microelastography is based on the use of OCT to measure tissue deformation in response to applied mechanical compression. In this feasibility study on 58 ex-vivo samples from patients undergoing mastectomy or wide local excision, these researchers demonstrated the performance of OCME as a means to visualize tissue micro-architecture in benign and malignant human breast tissues. Through a comparison with corresponding histology and OCT images, OCME is shown to enable ready visualization of features such as ducts, lobules, microcysts, blood vessels, and arterioles and to identify invasive tumor through distinctive patterns in OCME images, often with enhanced contrast compared with OCT. The authors concluded that these results laid the foundation for future intra-operative studies.
Chin and associates (2017) noted that surgical treatment of breast cancer aims to identify and remove all malignant tissue. Intra-operative assessment of tumor margins is, however, not exact; thus, re-excision is frequently needed, or excess normal tissue is removed. Imaging methods applicable intra-operatively could help to reduce re-excision rates while minimizing removal of excess healthy tissue. Optical coherence elastography (OCE) has been proposed for use in breast-conserving surgery; however, intra-operative interpretation of complex OCE images may prove challenging. Observations of breast cancer on multiple length scales, by OCE, ultrasound elastography, and atomic force microscopy, have shown an increase in the mechanical heterogeneity of malignant breast tumors compared to normal breast tissue. In this study, a micro-scale mechanical heterogeneity index is introduced and used to form heterogeneity maps from OCE scans of 10 ex-vivo human breast tissue samples. Through comparison of OCE, OCT images, and corresponding histology, malignant tissue is shown to possess a higher heterogeneity index than benign tissue. The authors concluded that the heterogeneity map simplified the contrast between tumor and normal stroma in breast tissue, facilitating the rapid identification of possible areas of malignancy, which is an important step towards intra-operative margin assessment using OCE.

Polarization-Sensitive Optical Coherence Tomography:

Patel et al (2014) noted that intra-operative delineation of breast cancer is a significant problem in surgical oncology. A reliable method for demarcation of malignant breast tissue during surgery would reduce the re-excision rate due to positive margins. These researchers presented a novel method of identifying breast cancer margins using combined dye-enhanced
wide-field fluorescence polarization imaging for en face cancer margins and polarization-sensitive (PS)-OCT for cross-sectional evaluation. Tumor specimens were collected following breast surgery, stained with methylene blue, and imaged. Wide-field fluorescence polarization images were excited at 640 nm and registered between 660 and 750 nm. Standard and PS-OCT images were acquired using a commercial 1,310-nm swept-source system. The imaging results were validated against histopathology. Statistically significant higher fluorescence polarization of cancer as compared with both normal and fibrocystic tumor tissue was measured in all the samples. Fluorescence polarization delineated lateral breast cancer margins with contrast superior to that provided by OCT. However, OCT complemented fluorescence polarization imaging by facilitating cross-sectional inspection of tissue; PS-OCT yielded higher contrast between cancer and connective tissue, as compared with standard OCT. The authors concluded that combined PS-OCT and fluorescence polarization imaging showed promise for intra-operative delineation of breast cancer. These preliminary findings need to be validated by well-designed studies.

South and colleagues (2014) noted that successful treatment of breast cancer typically requires surgical removal of the tumor; and OCT has been previously developed for real-time imaging of the surgical margin. However, it can be difficult to distinguish between normal stromal tissue and cancer tissue based on scattering intensity and structure alone; PS-OCT is sensitive to form birefringence of biological tissue. These investigators reported on the development of a high-speed PS-OCT system and imaging of ex-vivo human breast tissue, showing enhanced contrast between healthy and cancerous tissues based upon collagen content confirmed with corresponding histology. The
authors concluded that these results demonstrated the feasibility of using PS-OCT to supplement structural OCT as a possible method for intra-operative tumor margin evaluation.

Prostatectomy:

Yoon and colleagues (2016) noted that preservation of prostatic nerves is critical to recovery of a man's sexual potency after radical prostatectomy. A real-time imaging method of prostatic nerves will be helpful for nerve-sparing radical prostatectomy (NSRP); PS-OCT, which provides both structural and birefringent information of tissue, was applied for detection of prostatic nerves in both rat and human prostate specimens, ex-vivo. PS-OCT imaging of rat prostate specimens visualized highly scattering and birefringent fibrous structures superficially, and these birefringent structures were confirmed to be nerves by histology or multi-photon microscopy (MPM). PS-OCT could easily distinguish these birefringent structures from surrounding other tissue compartments such as prostatic glands and fats. PS-OCT imaging of human prostatectomy specimens visualized 2 different birefringent structures, appearing fibrous and sheet-like. The fibrous ones were confirmed to be nerves by histology, and the sheet-like ones were considered to be fascias surrounding the human prostate. PS-OCT imaging of human prostatectomy specimens along the perimeter showed spatial variation in the amount of birefringent fibrous structures, which was consistent with anatomy. The authors concluded that these findings demonstrated the feasibility of PS-OCT for detection of prostatic nerves. They stated that the next step will be pre-clinical study with animal models. For that, the current system will be miniaturized for in-vivo imaging of rat model or for translating PS-OCT as an imaging guide during NSRP by implementing a
laparoscopic OCT probe that can do both wide-field imaging and PS-OCT. Furthermore, real-time PS-OCT displaying technique in both cross-sectional and en face views will be developed for rapid nerve detection during surgery.

Vogt-Koyanagi-Harada (VKH) Disease:

Miura and colleagues (2017) stated that Vogt-Koyanagi-Harada (VKH) disease is a systemic autoimmune disorder that affects organs with melanocytes. The sunset glow fundus (SGF) in VKH disease was evaluated with PS-OCT. The study involved 28 eyes from 14 patients with chronic VKH disease, 21 eyes from 21 age-matched controls, and 22 eyes from 22 high-myopic patients with a tessellated fundus. VKH eyes were grouped into sunset or non-sunset groups on the basis of color fundus images. The presence of melanin in the choroid was determined by using the degree of polarization uniformity (DOPU) obtained by PS-OCT. The sunset glow index (SGI) was calculated by using color fundus images. Presence of an SGF was evaluated by using DOPU, SGI, sub-foveal choroidal thicknesses, near-infrared images, and auto-fluorescence images at 488-nm (SW-AF) and 785-nm (NIR-AF). There were 16 eyes in the sunset group and 12 eyes in the non-sunset group. For all eyes in the sunset group, the disappearance of choroidal melanin was clearly detected with PS-OCT. Percentage areas of low DOPU in the choroidal interstitial stroma of the sunset group were significantly lower than those of other groups and showed no overlap with other groups. The distribution of choroidal thicknesses and SGI in the sunset group substantially overlapped with other groups. The subjective analyses of the sunset and non-sunset groups, using near infrared, SW-AF, or NIR-AF, showed substantial inconsistencies with the PS-OCT results. The authors concluded that the findings of this study
showed the clinical usefulness of PS-OCT to evaluate the SGF in VKH disease, and DOPU measurement with PS-OCT could non-invasively evaluate choroidal melanin content and may have the potential for the clinical assessment of chronic VKH disease. However, PS-OCT is not yet commercially available for widespread use and maintenance and operation of PS-OCT systems is more complicated than for commercialized standard OCT. Moreover, they stated that further study is needed to confirm the possible use of PS-OCT for chronic VKH disease.

This study had several drawbacks: (i) with the relatively small number of patients (28 eyes from 14 patients), this trial evaluated only some aspects of sunset glow appearance. To evaluate the development of the SGF, a long-term observational study from the onset of the intra-ocular inflammation is needed, (ii) it should also be noted that choroidal melanin content is affected by ethnic differences. Since this study only evaluated Japanese patients, future research projects should examine if these findings extend to other ethnicities, and (iii) although a previous histologic study has indicated that human choroidal melanin tends to decrease with age, these researchers did not observe in the present study any significant correlation between the percentage area of low DOPU and age in any of the groups. Furthermore, although there is evidence that a monotonic relationship exists between DOPU and melanin, the nature of this relationship remains poorly understood and is seldom investigated.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

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<th>Code</th>
<th>Code Description</th>
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http://qawww.aetna.com/cpb/medical/data/800_899/0886_draft.html 06/06/2018
<table>
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<td>CPT codes not covered for indications listed in the CPB:</td>
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<td><strong>Intra-hyphenoperative optical coherence tomography/microelastography for solid tumor, intra-hyphenoperative polarization-hyphensensitive optical coherence tomography - no specific code:</strong></td>
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<tr>
<td>0351T</td>
<td>Optical coherence tomography of breast or axillary lymph node, excised tissue, each specimen; real time intraoperative</td>
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<td>0352T</td>
<td>interpretation and report, real time or referred</td>
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<td>0353T</td>
<td>Optical coherence tomography of breast, surgical cavity; real time intraoperative</td>
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<td>C50.011 - C50.929</td>
<td>Malignant neoplasm of breast</td>
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<td>C61</td>
<td>Malignant neoplasm of prostate</td>
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<td>C64.1 - C64.9</td>
<td>Malignant neoplasm of kidney, except renal pelvis</td>
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<td>C71.0 - C71.9</td>
<td>Malignant neoplasm of brain</td>
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<tr>
<td>C72.0</td>
<td>Malignant neoplasm of spinal cord</td>
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Optical Coherence Tomography and Microelastography for Solid Tumors and Other Se...

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The above policy is based on the following references:


10. Esserman LJ, Joe BN. Diagnostic evaluation of women with suspected breast cancer. UpToDate Inc., Waltham, MA. Last reviewed May 2014.


16. Zysk AM, Chen K, Gabrielson E, et al. Intraoperative assessment of final margins with a handheld optical imaging probe during breast-conserving surgery may reduce the reoperation rate: Results of a


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Amendment to
Aetna Clinical Policy Bulletin Number: 0886 Optical Coherence
Tomography and Microelastography for Solid Tumors and Other
Selected Indications

There are no amendments for Medicaid.