Anthem

Medical Policy

Subject: Nanoparticle-Mediated Thermal Ablation
Document #: SURG.00161
Status: New

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Description/Scope

This document addresses the use of nanoparticle-mediated thermal ablation to treat solid tumors. Nanoparticles are instilled into tumor tissue and then exposed to an energy source. Nanoparticle vibration induced by the energy source increases temperature to ablate the targeted tissue. Nanoparticle-mediated thermal ablation is purported to achieve homogeneous heat distribution in tumor tissue while protecting surrounding healthy tissue.

Position Statement

Investigational and Not Medically Necessary:

Nanoparticle-mediated thermal ablation is considered **investigational and not medically necessary** for all indications.

Rationale

Magnetic field induction ablation

Grauer and colleagues (2019) reported on 6 individuals with recurrent glioblastoma who underwent intracavitary thermotherapy with nanoparticles subjected to alternating magnetic fields. Following tumor resection, the cavity walls were coated with 2 or 3 layers of NanoTherm® particles. A total of 6 semi-weekly thermotherapy sessions were conducted using an alternating magnetic field applicator. Radiotherapy was given concurrently to the 4 individuals who were eligible for that treatment. Perifocal edema around the nanoparticle deposits developed in all participants approximately 2 to 5 months following treatment. This response resulted in headaches or worsening of pre-existing focal neurological deficits in 4 of the 6 study participants. These 4 individuals required treatment with high dose dexamethasone and additional surgery to remove the nanoparticles and the adjacent granulation tissue. Individuals treated at first recurrence (n=3) had a median overall survival (OS) of 23.9 months, The median OS in the individuals treated at the 2nd or 4th recurrence was 7.1 months. The authors concluded that a prospective phase I trial is warranted.

Nanoparticle-mediated thermal ablation has also been proposed as a treatment for prostate cancer, but there are no published studies to support this proposal. A single arm, prospective clinical trial using NanoTherm® (MagForce® AG, El Monte, CA) is underway to evaluate this therapy in individuals with intermediate-risk prostate cancer under active observation (NCT05010759). The estimated primary completion date is June 2023.

The National Comprehensive Cancer Network Guidelines in Oncology (NCCN Guidelines®) do not recommend nanoparticle-mediated thermal ablation as a treatment for any condition. There is insufficient published evidence to permit reasonable conclusions concerning the effect of nanoparticle-mediated thermal ablation for any condition.

Non-infrared light induction ablation

Rastinhad and associates (2019) published the results of a clinical pilot study which used gold nanoparticles and laser ablation to treat individuals with low- or intermediate-risk localized prostate cancer (n=16). Participants received an intravenous (IV) infusion of gold-silica nanoshells (GSN) that preferentially settled in the aberrant vasculature of the prostatic tumor. The prostate was then treated with a laser guided by magnetic resonance and ultrasound fusion imaging. The subablative laser dose did not harm tissue without GSN, but GSN excitation by the laser ablated the cancerous tissue. The full treatment was limited to 15 individuals, one individual dropped out after experiencing epigastric pain following the infusion of nanoparticles. Following treatment, these 15 participants had follow-up evaluation with imaging and/or biopsy at 48-72 hours, 3 months and 12 months post-procedure. At 3 months post-procedure, 60% of the participants were free of cancer in the ablation zone. At 12 months post-procedure, 86.7% of the participants were free of cancer in the ablation zone. There were no reported grade 3 or higher adverse effects (AEs). The authors note that this study was not powered to evaluate the efficacy of this treatment and cautioned that it would be premature to draw any conclusions about efficacy.

An open-label, multi-center, single-treatment pivotal study with up to 60 participants is currently underway (). Participants in the study include those with low- to intermediate-risk localized prostate cancer with MRI visible and confirmed focal areas of prostate cancer. The study is set to follow-up with individuals for 12 months following treatment.

Summary

There is insufficient evidence published in peer-reviewed medical literature to permits reasonable conclusions concerning the safety, efficacy, or improved net health outcomes of nanoparticle-mediated thermal ablation for any indication.

Background/Overview

Prostate cancer is the most common non-skin type of cancer in men in the United States (US). In 2023, there will be an estimated 288,300 new cases of prostate cancer and approximately 34,700 deaths attributed to prostate cancer. Following a prostate cancer diagnosis, the NCCN guidelines on prostate cancer (V1.2023)recommend that the choice between observation, active surveillance and definite treatment be made on several determinants, with the key determinant being life expectancy. Active surveillance is recommended for individuals in the very-low-risk and low-risk groups and a life expectancy of 10 or more years. Active surveillance is also recommended for individuals in the favorable intermediate risk category. These individuals may benefit from avoiding the side effects of definitive treatment for at least 10 years without adversely impacting cure rates. Approximately 32% to 50% of individuals in the active surveillance group will undergo treatment within 10 years. Individuals who choose active surveillance also incur very-low risk of progression to a regional or metastatic stage.

Nano-oncology therapies have been proposed as an alternative method to treat cancers. Nanomedicine techniques under

investigation include therapies using nanocarriers introduced through the vascular system to deliver therapeutic agents to the targeted area. Thermal nanoparticle therapy consists of the placement of inorganic materials to the target area followed by the application of an external energy source to cause vibration and hyperthermia (Nirmala, 2023).

Therapy is thought to attack tumor cells in several ways. The hyperthermia generated by nanoparticle vibration causes tumor cell death. Cancerous cells, which are more susceptible to cell death via hyperthermia due to their leaky vascular nature, would be more affected than healthy cells. Hyperthermia also increases tumor cell susceptibility to concomitant therapies, such as radiation or chemotherapy. It has also been postulated that local hyperthermia precipitated by alternating magnetic fields using magnetic nanoparticles may induce an antitumor immune response and trigger antitumor immunity and increase sensitivity to chemotherapy and immunotherapy (Grauer, 2019; Mahmoud, 2018).

The NanoTherm therapy consists of 3 components: NanoTherm® - a ferrofluid containing iron oxide particles, NanoActivator® - the alternating magnetic field generator, and NanoPlan® - the software that supports individual treatment plans. Following injection of NanoTherm®, the individual receives 6 treatment sessions over the course of 3 weeks. At this time in the US, studies are focused on intermediate stage prostate cancer. The goal of this focal treatment of small lesions is to allow individuals to remain in active surveillance and avoid the side effects of more invasive treatment.

AuroLase® Therapy (Nanospectra Biosciences, Houston TX) consists of nanoparticles with a gold metal shell and a non-conducting silica core that are delivered via IV and accumulate in the tumor. When exposed to photonic laser energy, the particles convert the light to heat destroying the tumor and the supplying vascular system without affecting adjacent tissue. The AuroShell particles are considered an investigational device at this time. Both therapies are considered investigational devices by the Food and Drug Administration (FDA) at this time.

Definitions

Active Surveillance: Disease monitoring with expectation of curative treatment if there is progression.

NanoTherm® particles: a colloidal suspension of amino silane coated with iron oxide nanoparticles suspended and distributed in 15 nm size particles.

Observation: Disease monitoring on a less intensive scale until symptoms develop or are thought to be imminent. Treatment may be curative or palliative.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
For the following procedure codes, or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT	
0738T	Treatment planning for magnetic field induction ablation of malignant prostate tissue, using data from previously performed magnetic resonance imaging (MRI) examination
0739T	Ablation of malignant prostate tissue by magnetic field induction, including all intraprocedural, transperineal needle/catheter placement for nanoparticle installation and intraprocedural temperature monitoring, thermal dosimetry, bladder irrigation, and magnetic field nanoparticle activation
	For the following unlisted codes when specified as nanoparticle thermal ablation:
55899	Unlisted procedure, male genital system [*when specified as nanoparticle thermal ablation*]
64999	Unlisted procedure, nervous system [*when specified as nanoparticle thermal ablation*]
ICD-10 Procedure	
0V503ZZ	Destruction of prostate, percutaneous approach [**when specified as** *nanoparticle thermal ablation*]
ICD-10 Diagnosis	
	All diagnoses

References

Peer Reviewed Publications:

1. Grauer O, Jaber M, Hess K, et al. Combined intracavitary thermotherapy with iron oxide nanoparticles and radiotherapy as local treatment modality in recurrent glioblastoma patients. J Neurooncol. 2019; 141(1):83-94.
2. Hao B, Wei L, Cheng Y, et al. Advanced nanomaterial for prostate cancer theranostics. Front Bioeng Biotechnol. 2022; 10:1046234.
3. Mahmoudi K, Bouras A, Bozec D, et al. Magnetic hyperthermia therapy for the treatment of glioblastoma: A review of the therapy's history, efficacy and application in humans. Int J Hyperthermia. 2018; 34(8):1316-1328.
4. Maier-Hauff K, Ulrich F, Nestler D, et al. Efficacy and safety of intratumoral thermotherapy using magnetic iron-oxide nanoparticles combined with external beam radiotherapy on patients with recurrent glioblastoma multiforme. J Neurooncol. 2011; 103(2):317-324.
5. Nirmala MJ, Kizhuveetil U, Johnson A, et al. Cancer nanomedicine: a review of nano-therapeutics and challenges ahead. RSC Adv. 2023; 13(13):8606-8629.
6. Rastinehad AR, Anastos H, Wajswol E, et al. Gold nanoshell-localized photothermal ablation of prostate tumors in a clinical pilot device study. Proc Natl Acad Sci U S A. 2019; 116(37):18590-18596.
7. Rodríguez F, Caruana P, De la Fuente N, et al. Nano-based approved pharmaceuticals for cancer treatment: Present and future challenges. Biomolecules. 2022; 12(6):784.

8. Schwake M, Müther M, Bruns AK, et al. Combined fluorescence-guided resection and intracavitary thermotherapy with superparamagnetic iron-oxide nanoparticles for recurrent high-grade glioma: Case series with emphasis on complication management. Cancers (Basel). 2022; 14(3):541.
9. Taneja SS. Re: Gold nanoshell-localized photothermal ablation of prostate tumors in a clinical pilot device study. J Urol. 2020; 203(1):31.
10. Zhao J, Zhang C, Wang W, Li C, Mu X, Hu K. Current progress of nanomedicine for prostate cancer diagnosis and treatment. Biomed Pharmacother. 2022; 155:113714.

Government Agency, Medical Society, and Other Authoritative Publications:

1. MagForce USA. Stage 2B of: A pivotal, prospective, three-stage, single-arm study of focal ablation of the prostate with NanoTherm® Therapy System for a limited-volume, clinically localized, intermediate-risk prostate cancer. NLM Identifier: NCT05010759. Last updated on August 24, 2022. Available at: https://clinicaltrials.gov/ct2/show/NCT05010759. Access on May 15, 2023.
2. Nanospectra Biosciences, Inc. An Extension Study MRI/US Fusion Imaging and Biopsy in Combination With Nanoparticle Directed Focal Therapy for Ablation of Prostate Tissue. NCT04240639. Last updated on July 19, 2022. Available at: https://clinicaltrials.gov/ct2/show/NCT04240639. Accessed on May 15, 2023.
3. NCCN Clinical Practice Guidelines in Oncology®. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on April 22, 2023.
   - Central Nervous System Cancers. V.1.2023. Revised March 24, 2023.
   - Prostate Cancer. V.1.2023. Revised September 16, 2022.

Websites for Additional Information

1. American Cancer Society. Prostate Cancer. Key Statistics for Prostate Cancer. Available at: https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html. Accessed on April 22, 2023.
2. National Cancer Institute (NCI). Cancer and Nanotechnology. Available at:https://www.cancer.gov/nano/cancer-nanotechnology. Accessed on April 22, 2023.

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The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
New	05/11/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Initial document development.

Applicable to Commercial HMO members in California: When a medical policy states a procedure or treatment is investigational, PMGs should not approve or deny the request. Instead, please fax the request to Anthem Blue Cross Grievance and Appeals at fax # 818-234-2767 or 818-234-3824. For questions, call G&A at 1-800-365-0609 and ask to speak with the Investigational Review Nurse.

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.