FDA Executive Summary

Prepared for the

Fall 2026 review by the

FDA's Pediatric Advisory Committee

H190003

Sonalleve MR-HIFU System

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I. INTRODUCTION

In accordance with the Pediatric Medical Device Safety and Improvement Act, this review provides a safety update based on the post-market experience with the use of the Sonalleve MR-HIFU (Magnetic Resonance – High Intensity Focused Ultrasound) System as a treatment for osteoid osteomas in the extremities of pediatric patients.

The Sonalleve MR-HIFU System is designed to non-invasively deliver acoustic energy to targeted anatomy. The system combines a high energy ultrasound transducer, an MR imaging system, and a targeting system to deliver position and time-controlled ultrasound energy. The focused ultrasound energy raises tissue temperatures until the targeted tissue is ablated. MR-guided HIFU treatment is an image-guided technique combining High Intensity Focused Ultrasound with real-time monitoring of temperature change during the sonication.

The purpose of this review is to provide the Pediatric Advisory Committee (PAC) with post-market safety data, so that the committee can advise the Food and Drug Administration (FDA) on any probable safety concerns associated with the use of this device in children. This executive summary will include summaries of the pre-market clinical study, post-market experience in a completed pivotal study, the peer-reviewed literature associated with the device, and post-market medical device reporting for adverse events. This executive summary provides updated information covering data from November 2021 to April 2026.

II. INDICATIONS FOR USE

The Sonalleve MR-HIFU System is intended to be used for the treatment of osteoid osteomas in the extremities.

III. BRIEF DEVICE DESCRIPTION

The Sonalleve MR-HIFU System (Figure 1) is designed to non-invasively deliver acoustic energy to prescribed locations. The system integrates a high intensity phased array focused ultrasound transducer with an MR-imaging system and electromechanical transducer positioning system to deliver spatially and temporally controlled ultrasound energy to elevate tissue temperatures, and to ablate tissues non-invasively.

The Sonalleve MR-HIFU System is designed to be used with Philips Achieva and Ingenia 1.5T and 3.0T MR scanners and complies with the requirements of the applicable International Electrotechnical Commission (IEC) safety standards.

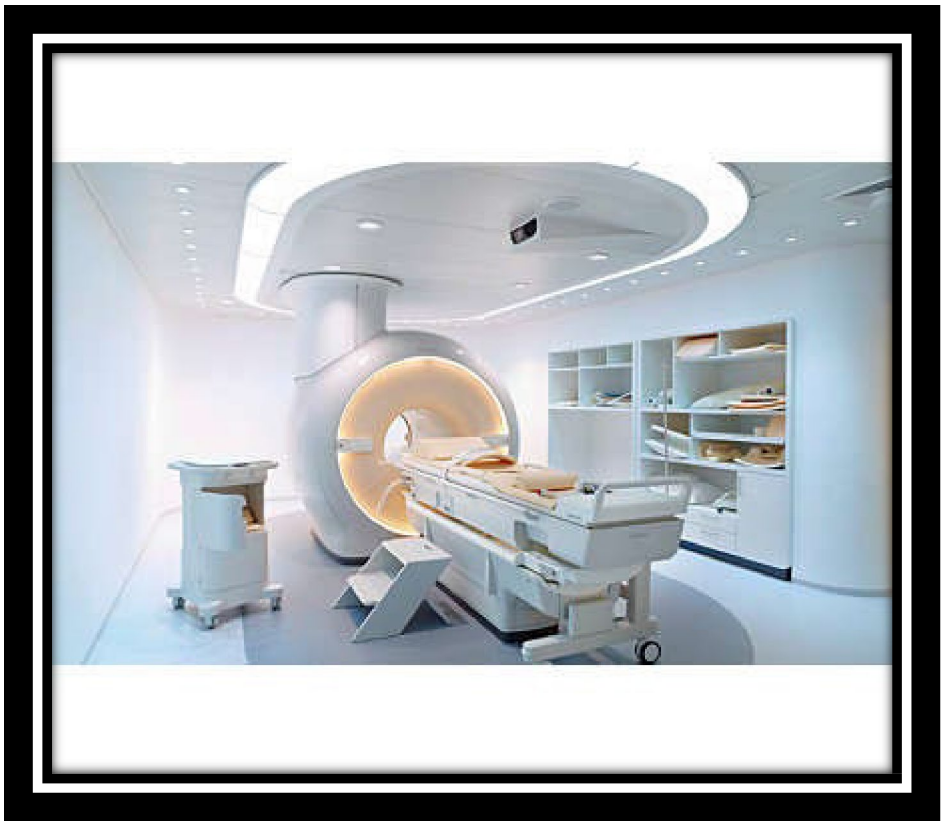

Figure 1: Sonalleve MR-HIFU System

The Sonalleve MR-HIFU System consists of the following main components:

- Sonalleve Patient Table assembly - The Sonalleve Patient Table is a mobile patient support used for MR-HIFU Therapy in an Achieva or Ingenia medical diagnostic MR system. The Patient Table is positioned to sit above the standard MR system Patient Support. It can be removed to enable normal diagnostic use of the MR scanner. The Sonalleve Patient Table (denoted as "HIFU TABLE" in Figure 2) and its parts (see below) are located in the examination room within the patient environment.
    - Ultrasound transducer
    - Positioning mechanics
    - Matching electronics
    - Connector panel
    - Sonalleve Pelvis coil
    - Patient Emergency Stop Button
    - Pads, mattresses, and straps for patient positioning
    - Direct skin cooling device

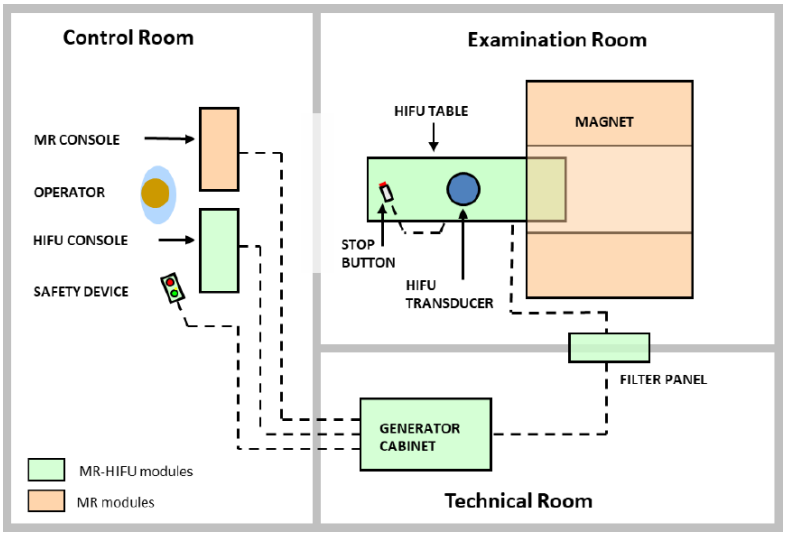

Figure 2: Schematic of main components of Sonalleve MR-HIFU System

- Sonalleve Generator Cabinet - The Sonalleve MR-HIFU System requires a separate cabinet for power distribution and the control driver electronics of the ultrasound transducer. The Sonalleve Generator Cabinet and its parts are located in the technical room. Electrically shielded cables connect the Generator Cabinet to the Patient Tabletop through a dedicated HIFU filter panel on the wall between the technical and examination rooms.

- Sonalleve Therapy Planning Console with a Safety Device - The Sonalleve Console is used for transferring the planning images from the MR scanner, planning the sonication treatment, and the actual therapy sonication. It is located in the control room, with direct visibility to the examination room. A monitor and safety device are included with the Sonalleve Console. The operator can terminate the treatment at any point using the Safety Device if the operator detects a hazardous situation as an undesired heating pattern, or a malfunction in the equipment.

IV. REGULATORY HISTORY

On December 18, 2018, the Sonalleve MR-HIFU System received designation as a Humanitarian Use Device (HUD). On November 27, 2020, the Humanitarian Device Exemption (HDE) application was approved by the Center for Devices and Radiological Health of the FDA.

V. PRE-MARKET DATA: CLINICAL INVESTIGATION

Summary of Clinical Study:

The Sonalleve MR-HIFU System was reviewed under Investigational Device Exemption (IDE) submission G130041 and associated supplements. The device was studied for the ablation of osteoid osteomas in children and young adults in a feasibility study entitled “Safety and Feasibility of MR-Guided High Intensity Focused Ultrasound (MR-HIFU) Ablation of Osteoid

Osteoma in Children" (ClinicalTrials.gov Identifier: NCT02349971). Nine patients were treated in this study.

Purpose / Objective of Study

The primary endpoints of safety and effectiveness were determined through clinical assessments and evaluation of toxicity, and measurable clinical response (pain, distress, and quality of life) and imaging response at 12 months. These included Visual Analogue Scale (VAS), Symptom Distress Scale (SDS), Patient-Reported Outcomes Measurement Information System score and Pediatric Quality of Life Inventory (v 4.0). In addition, pain medication or non-steroidal anti-inflammatory drug (NSAID) use (frequency and dose) were recorded for the five days prior to treatment and for up to thirty days (or longer if needed) following treatment and compared. Feasibility was determined through technically successful completion of treatment.

Adverse Events

In total, 16 adverse events were reported in the Osteoid Osteoma study. No serious adverse events were reported. Two of the nine treated subjects did not experience any adverse events. All adverse events were transitory. One patient developed minor focal bruising at the edges of the treatment window, which was attributed to inadequate padding at this location. This bruising was visible but caused minimal discomfort and resolved without additional treatment within one week. The complete list of reported adverse events in the Osteoid Osteoma study is presented in Table 1 below:

Subject ID	Adverse Event	Relationship to Study Device	Grade	Serious adverse event
OO27-0001	Fatigue	Possibly	Mild	No
	Leg pain	Probably	Moderate	No
	Nausea	Unlikely	Mild	No
OO27-0002	Bruising (bilateral shins)	Unlikely	Mild	No
	Leg pain	Possibly	Moderate	No
OO27-0003	Leg pain	Probably	Moderate	No
OO27-0005	Muscle pain	Probably	Mild	No
	Nausea	Unlikely	Mild	No
OO27-0006	Foot pain	Possibly	Mild	No
	Laryngeal inflammation	Unlikely	Mild	No
	Back pain	Unlikely	Mild	No
OO27-0008	Headache	Not related	Moderate	No
	Back pain	Not related	Moderate	No
	Nausea	Not related	Mild	No
OO27-009	Peripheral sensory neuropathy	Unlikely	Mild	No
	Peripheral motor neuropathy	Unlikely	Mild	No

Table 1: Reported adverse events in the Osteoid Osteoma feasibility study

Summary of Results

Patient reported outcomes, including pain reduction and improvement in quality of life, showed significant overall improvement ($P = 0.0002$, Friedman non-parametric test). Pain resolution was demonstrated by improvement in the median VAS score, which decreased from 6 to 0 ($P < 0.01$, Dunn post hoc test) by day 28 after HIFU treatment. There was clear reduction in NSAID use; 8 of 9 patients were no longer taking medication after HIFU therapy. Furthermore, patients reported improvement in sleep quality following treatment. Pain-associated sleep interruption decreased significantly following MR-HIFU ablation ($P = 0.0013$, Friedman). The number of patients with pain-related sleep disruption decreased from 8 to 1. Additional patient reported outcome results are presented in the H190003 Summary of Safety and Probable Benefit (https://www.accessdata.fda.gov/cdrh_docs/pdf19/H190003B.pdf).

Conclusion

The results showed that MR-HIFU ablation of painful osteoid osteoma can provide improved patient reported outcomes and lasting pain resolution. No serious treatment-related adverse events were observed in any of the 9 patients who underwent MR-HIFU. All treatments were performed on an outpatient basis without overnight admission. The minor focal bruising due to inadequate padding at edges of the HIFU treatment window can be addressed by ensuring that adequate padding and careful positioning are applied.

MR-HIFU ablation was feasible in all 9 patients who consented to this treatment. The single patient with partial clinical response following MR-HIFU ablation had an osteoid osteoma

located in the medullary cavity of the femur, rather than the cortex. Post-treatment MRI in this patient showed that periosteal nerves were ablated but the nidus remained viable. This explains partial improvement, but not complete resolution, of symptoms in this patient at the 1-month follow-up assessment. This patient later underwent radiofrequency ablation (RFA). On the other hand, one patient who had previously undergone unsuccessful surgical resection and RFA demonstrated a complete clinical response after MR-HIFU ablation.

VI. POST-MARKET DATA: ANNUAL DISTRIBUTION NUMBER

Section 520(m)(6)(A)(ii) of the Food, Drug, and Cosmetic Act (FD&C Act) allows HDEs indicated for pediatric use to be sold for profit as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). On December 13, 2016, the 21st Century Cures Act (Pub. L. No. 114-255) updated the definition of ADN to be the number of devices "reasonably needed to treat, diagnose, or cure a population of 8,000 individuals in the United States." Profound Medical Inc. provided confirmation on March 23, 2026, that 20 was the maximum ADN. No additional Sonalleve MR-HIFU System devices have been shipped or sold since the initial approval of H190003.

Following HDE approval, Profound Medical Inc. treated 15 patients under a pivotal study for ablation of painful osteoid osteoma in children and young adults (ClinicalTrials.gov Identifier: NCT04658771) as approved in IDE G130041/S022. All 15 patients completed their participation in the study, which will be closed in the coming months following completion of data analysis (ClinicalTrials.gov has not been updated and still identifies an estimated study completion date of December 30, 2025). No serious adverse events or unanticipated device-related adverse events have been reported in this study.

An application for the Sonalleve MR-HIFU System for the treatment of osteoid osteoma received CE mark in August 2020. One serious adverse event was reported in the European Union (EU) for treatment of osteoid osteoma using the Sonalleve MR-HIFU System. The patient experienced a complete rupture of the flexor digitorum profundus tendon approximately 6 weeks after treatment of an adjacent osteoid osteoma. The patient underwent successful surgical reconstruction. It is unclear whether this event was related to the treatment or to the underlying tumor as pre-treatment MRI showed tendinosis/tendinitis. Given uncertainties associated with this isolated case report, there is no significant change to the overall benefit-risk profile of the Sonalleve MR-HIFU System.

VII. SYSTEMATIC LITERATURE REVIEW OF SAFETY IN THE PEDIATRIC POPULATION

Purpose

In preparation for the FDA PAC 2026 fall meeting, a literature review was conducted to address the following question: what adverse events are reported in the literature associated with the use of MR-HIFU for any indication in the pediatric population (<22 years old).

Methods

A PubMed, Google Scholar, and web-search literature search was performed covering the period between 2013 and 2026. The HDE was approved on November 27, 2020. In addition, ongoing clinical trials (clinicaltrials.gov) were also reviewed.

Discussion

A literature search yielded the following distribution of articles by year for a total of 55 articles: 2011 (1), 2013 (2), 2014 (1), 2015 (1), 2016 (3), 2017 (3), 2018 (5), 2019 (4), 2020 (3), 2021 (8), 2022 (6), 2023 (6), 2024 (12), 2025 (5), and 2026 (1). Eight clinical trials related to osteoid osteoma were identified in the ClinicalTrials.Gov database. Three of these trials were conducted in the United States, with one previously completed and two with expected completion dates within this reporting period. Of the five trials conducted outside the United States, two are completed, one is recruiting, one was terminated, and one is of unknown status. Finally, information describing the applicant's clinical experience with the device since HDE approval was requested including safety data generated from post-market studies, and information (whether published or unpublished) that affects an evaluation of the safety of the device or that affects the statement of contraindications, warnings, precautions, and adverse reactions in the device's labeling.

Conclusion

Four clinical trials related to osteoid osteoma remain active since the last PAC Meeting. Three of these trials (NCT02923011, NCT04803773, DRKS00015448), unrelated to the Sonalleve MR-HIFU System, are recruiting, including one in the US (NCT02923011).

No new safety concerns or signals specific to the Sonalleve MR-HIFU System have been identified in the published literature.

VIII. MEDICAL DEVICE REPORTS

Overview of Manufacturer and User Facility Device Experience Database

Each year, the FDA receives several hundred thousand MDRs of suspected device-associated deaths, serious injuries, and malfunctions. The FDA database houses MDRs submitted to the FDA by mandatory reporters (manufacturers, importers, and device user facilities) and voluntary reporters such as health care professionals, patients, and consumers. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products. MDRs can be used effectively to:

- Establish a qualitative snapshot of adverse events for a specific device or device type
- Detect actual or potential device problems used in a "real world" setting/ environment, including:
    - rare, serious, or unexpected adverse events
    - adverse events that occur during long-term device use

- adverse events associated with vulnerable populations
- off-label use
- use error

Although MDRs are a valuable source of information, this passive surveillance system has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about frequency of device use. Because of this, MDRs comprise only one of the FDA's several important post-market surveillance data sources. Other limitations of MDRs include, but are not necessarily limited to:

- MDR data alone cannot be used to establish rates of events, evaluate a change in event rates over time, or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices.
- Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report. Establishing a cause-and-effect relationship is especially difficult if circumstances surrounding the event have not been verified or if the device in question has not been directly evaluated.
- MDR data are subject to reporting bias, attributable to potential causes such as reporting practice, increased media attention, and/or other agency regulatory actions.
- MDR data do not represent all known safety information for a reported medical device and should be interpreted in the context of other available information when making device-related or treatment decisions.

MDRs Associated with the Sonalleve MR-HIFU System

An MDR search for brand name ‘Sonalleve’ and manufacturer name ‘Profound’ in the MDR database returned one MDR for the device. This MDR described an event that occurred in the EU and is summarized in Section VI above.

MDR Summary

Given uncertainties with the isolated case report described in the identified MDR, the MDR search raised no new safety concerns.

IX. SUMMARY

Since approval of the HDE for the Sonalleve MR-HIFU System, Profound Medical Inc. treated fifteen patients in a pivotal study. These fifteen patients received seventeen treatments in total including two re-treatments, and all have completed their participation in the study. This approved pivotal study (G130041/S022) is for treatment of painful osteoid osteoma in children and young adults (Osteoid Osteoma phase II). Our review of the published literature and MDRs since the time of approval of the HDE has not identified any new or unexpected risks for the pediatric population when compared to the premarket data.

FDA concludes that the Sonalleve MR-HIFU System, intended to be used for the treatment of osteoid osteomas in the extremities, does not pose an unreasonable or increased risk of illness or injury, and that the probable benefit to health continues to outweigh the risk of injury or illness. Accordingly, FDA recommends continued surveillance and will report the following to the PAC in 2027:

- Annual distribution number
- Literature review
- MDR review