O.N. Diagnostics, LLC.
% Mr. David Kopperdahl
Director, Research and Development
2150 Shattuck Ave., Suite 610
BERKELEY CA 94704

August 3, 2018

Re: K171435
Trade/Device Name: VirtuOst Vertebral Fracture Assessment
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture archiving and communications system
Regulatory Class: II
Product Code: LLZ
Dated: July 30, 2018
Received: August 2, 2018

Dear Mr. Kopperdahl:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see

https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Michael D. O'Hara For

Robert Ochs, Ph.D.
Director
Division of Radiological Health
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K171435

Device Name

VirtuOst Vertebral Fracture Assessment

Indications for Use *(Describe)*

VirtuOst VFA uses sagittal sections from a spine-containing CT scan, with or without contrast enhancement, to visualize and measure vertebral deformities, classify the type and grade of any existing vertebral fracture, and from this identify patients at high risk of a future osteoporosis-related fracture. This information can be interpreted by a physician to diagnose existing vertebral fractures and to manage patients for osteoporosis.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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C. 510(K) SUMMARY

Date: July 30, 2018

1) Applicant Information

510(k) Owner: O. N. Diagnostics, LLC
2150 Shattuck Ave. Suite 610
Berkeley, CA 94704

Contact Person: David Kopperdahl
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Establishment Reg. No.: 3010687441

2) Device Identification

Trade Name:	VirtuOst Vertebral Fracture Assessment
Common Name:	Vertebral Fracture Assessment
Regulatory Class:	II
Primary Classification Name:	Picture archiving and communications system
Primary Regulation Number:	21 CFR 892.2050
Primary Product Code:	LLZ
Secondary Classification Name:	Bone Densitometer
Secondary Regulation Number:	21 CFR 892.1170
Secondary Product Code:	KGI

3) Identification of Predicate Devices

K103475:	SpineAnalyzer
Company:	Optasia Medical
Primary Classification Name:	Picture archiving and communications system
Primary Regulation Number:	21 CFR 892.2050
Primary Product Code:	LLZ
K023554:	Dual-Energy Vertebral Assessment View Software Option
Company:	GE Lunar
Primary Classification Name:	Bone Densitometer
Primary Regulation Number:	21 CFR 892.1170
Primary Product Code:	KGI

4) Device Description

VirtuOst Vertebral Fracture Assessment (VFA) software is used to perform vertebral morphometry and is an integrated component of VirtuOst (K113725). VirtuOst VFA accepts as input a sagittal section of a vertebral body, obtained from a spine-containing computed tomography (CT) scan, and provides semi-automated, interactive tools with which the user can perform six-point quantitative vertebral morphometry according to well-established guidelines. The process can be repeated for multiple vertebral bodies. For each vertebral body analyzed, the quantitative vertebral morphometry algorithm locates three points each along the superior and inferior endplate on a sagittal section through the vertebra, typically a mid-sagittal section. The user verifies or modifies point placement. Based on these six morphometry points, anterior, posterior and middle vertebral heights are measured. Percent deformities are calculated from these heights and are then compared against well-established criteria for vertebral deformities typical of osteoporosis-related vertebral fracture in order to classify types and grades of any existing osteoporosis-related vertebral fracture, from which a patient can be classified as being at high risk of a future osteoporosis-related fracture. The VFA algorithm can be applied to any complete vertebral body captured in the CT scan, and the scan can be contrast-enhanced or not. Consistent with the recommended use of the well-established fracture-classification criteria, deformity types and fracture grades and fracture-risk classifications are only reported for vertebral levels T4 through L4. A report is generated containing these results, along with images of the sagittal sections from which the measurements were acquired. A physician then interprets the report to make any medical diagnoses or treatment decisions.

5) Intended Use

VirtuOst VFA uses sagittal sections from a spine-containing CT scan, with or without contrast enhancement, to visualize and measure vertebral deformities, classify the type and grade of any existing vertebral fracture, and from this identify patients at high risk of a future osteoporosis-related fracture. This information can be interpreted by a physician to diagnose existing vertebral fractures and to manage patients for osteoporosis.

6) Substantial Equivalence

Summary of Technology Characteristics and Comparison with Predicate Devices
The VirtuOst VFA software application is used in bone densitometry to provide measurements of existing vertebral deformities, classifications of the type and grade of any existing fractures, and a fracture-risk classification for a future osteoporosis-related fracture; it is substantially equivalent to predicate devices K103475 and K023554. VirtuOst VFA and the predicate devices are all software applications for use in bone densitometry, are all regulated as Class II devices, and all have substantially similar intended uses: to provide measurements of vertebral deformities for a physician to use in the diagnosis of vertebral fracture and the management of osteoporosis. All three devices have the same intended patient population — those who may be at elevated risk for an osteoporosis-related fracture.

The general methodology for performing the vertebral fracture assessment is substantially the same for VirtuOst VFA and the two predicate devices. All devices can be applied to the T4 through L4 vertebral levels to measure existing vertebral deformities among any or all of those levels, and these deformities are then classified as different grades (normal, mild, moderate,

severe) and types of vertebral fracture (anterior wedge, biconcavity, crush), if not normal. All devices rely on the same well-established "Genant" classification scheme for typical osteoporosis-related vertebral fracture, as described in the literature. In particular, six-point morphometry is used to measure anterior, middle and posterior heights of a vertebral body; various deformity ratios are then calculated from these heights and used to estimate percent deformities; these percentages are then compared against pre-established thresholds to classify the fracture type and grade of any existing osteoporosis-related fracture. All three devices also allow the user to enter the results of a semiquantitative visual assessment of vertebral deformities. These results and select images of the bone are displayed in a medical report. A physician then interprets this information to make any medical diagnosis and treatment decision.

A side-by-side comparison of the technology characteristics of VirtuOst VFA and the predicate devices demonstrates the similarity of the devices (**Table 1**). These characteristics have been grouped into four main workflow steps as follows:

Step 1 - Accept an x-ray-based image of the spine as input.
Step 2 - Locate and label the vertebrae of interest.
Step 3 - Perform 6-point quantitative vertebral morphometry.
Step 4 - Generate a report.

Table 1: Side-by-side comparison of the vertebral morphometry steps implemented by VirtuOst VFA and its predicates.

Feature	**VirtuOst VFA**	**SpineAnalyzer**	**DVA**
Step 1 - Accept an x-ray-based image of the spine as input.			
Input Image File Type	DICOM	DICOM or TIFF	Proprietary images from Lunar scanners.
Imaging Modality	CT	DXA and digital X-ray	DXA, SXA
Image format	Planar (sagittal section)	Planar (projection)	Planar (projection)
Step 2 - Locate and label the vertebrae of interest.			
Target Anatomy	Spine (Lateral) T4-L4	Spine (Lateral) T4-L4	Spine (Lateral & AP) T4-L4

Feature	VirtuOst VFA	SpineAnalyzer	DVA
Method for locating vertebra	Semi-automatic: An active contour segmentation routine seeded by a user mouse click on the vertebral body creates a segmentation mask of the sagittal section. The six points for vertebral morphometry are located automatically on the edges of this mask. Tools provided for manual adjustment.	Semi-automatic: 95-point segmentation routine seeded by a user mouse click on the vertebral body locates the extents of the bone. The six points for vertebral morphometry are located automatically using this contour. Tools provided for manual adjustment.	Semi-automatic: Proprietary segmentation routine initiated by user mouse click in the vertebral body. Image processing tools provided for manual adjustment. Automatic: Proprietary routine assumes image starts in sacrum. Image processing tools provided for manual adjustment.
Label Vertebral Levels	Manual	Manual	Manual or Automatic
Step 3 - Perform 6-point quantitative vertebral morphometry.			
Quantitative Morphometry Technique	Six-point morphometry	Six-point morphometry	Six-point morphometry
Vertebral Heights	Anterior Middle Posterior	Anterior Middle Posterior	Anterior Middle Posterior
Deformity Types	Wedge Biconcavity Crush	Wedge Biconcavity Crush	Wedge Biconcavity Crush
Deformity Grades	Grade 0: Normal Grade 1: Mild Grade 2: Moderate Grade 3: Severe	Grade 0: Normal Grade 1: Mild Grade 2: Moderate Grade 3: Severe	Grade 0: Normal Grade 1: Mild Grade 2: Moderate Grade 3: Severe
Percent Deformation	Expressed as a percentage equal to 100*(1-ratio), e.g. a ratio in heights of 0.75 is reported as a 25% deformation.	Expressed as a percentage equal to 100*(1-ratio), e.g. a ratio in heights of 0.75 is reported as a 25% deformation.	Expressed as a percentage equal to 100*(ratio), e.g. a ratio in heights of 0.75 is reported as a 75% deformation.

Feature	VirtuOst VFA	SpineAnalyzer	DVA
Fracture Thresholds	Threshold for fracture grade deformation based on the percent deformation: Grade 0: <20% Grade 1: ≥20 to <25% Grade 2: ≥25 to <40% Grade 3: ≥40%	Threshold for fracture grade deformation based on the percent deformation: Grade 0: <20% Grade 1: ≥20 to <25% Grade 2: ≥25 to <40% Grade 3: ≥40%	Threshold on the percent deformation as number of standard deviations below normal: Grade 0: <2 SD Grade 1: <3 SD Grade 2: <4 SD Grade 3: ≥4 SD Percentage-based thresholds can also be input by user.
Genant Semi-quantitative Assessment	Performed manually by user.	Performed manually by user.	Performed manually by user.
Step 4 - Generate a report.			
Morphometry Results	Percent deformation Deformity types Deformity grades If semiquantitative analysis performed, both quantitative and semiquantitative morphometry results are reported.	Percent deformation Deformity types Deformity grades If semiquantitative analysis performed, both quantitative and semiquantitative morphometry results are reported.	Percent deformation Deformity types Deformity grades If semiquantitative analysis performed, results replace quantitative morphometry results.
Images	Lateral view of the sagittal section of the vertebral body.	Lateral projection of the vertebral body.	Lateral projection of the vertebral body. AP projection if AP deformities assessed.
Image Annotation	Vertebral level labels and the six morphometry points.	Vertebral level labels and the six morphometry points.	Vertebral outlines and level labels and the six morphometry points.

Feature	VirtuOst VFA	SpineAnalyzer	DVA
Interpretation	Space available on report for clinician's narrative. Automatic fracture determination included on report. The Instructions for Use indicate that this is morphometry-based and not intended to replace "clinical judgment."	Space available on report for clinician's narrative. Automatic fracture determination included on report. The Instructions for Use indicate that this is morphometry-based and not intended to replace "clinical judgment."	Space available on report for clinician's narrative.

Summary of Clinical and Non-Clinical Performance Data

A clinical study of n=40 women and men was conducted to measure the repeatability and precision of VirtuOst VFA measurements. We used computed tomography scans acquired as part of standard care for 7000 women and men age 65 and older. From this resource, we found 716 patients who had two CT exams within a 90-day period, both with at least one reconstruction with a slice thickness of 1.25mm. A lateral projection of each CT image was then viewed in order to qualitatively identify candidate scans with spine fractures. From those patients with potential fracture, thirty-five were consecutively selected for inclusion in the study. To ensure that the precision cohort would include patients without fracture, we also selected five more from patients not flagged as having a potential fracture, for a total cohort of n=40.

Two operators performed vertebral fracture assessment on each patient's baseline CT scan using VirtuOst VFA. We then replaced all scan IDs with new IDs and randomized the scan order. After a minimum five-day wash-out period, one operator repeated the analysis of the baseline scans, and the other performed VFA of each patient's follow-up scan. Operators were blinded to each other's results as well as to their own first-pass results. From these data, intra-operator, interoperator, short-term (baseline vs. follow-up measurement by a single operator) and combined (baseline measurement by one operator vs. follow-up measurement by a second operator) precision were calculated.

As a reference standard, vertebral heights were also manually measured from high resolution (0.5 mm) printouts of midsagittal sections of the L1 vertebra from each CT scan. Height ratios were calculated and fracture grades assigned using six-point morphometry methods as described above. By these measurements, twenty-eight patients had a vertebral fracture at L1.

To address the influence of slice thickness on VirtuOst VFA results, we resampled the 40 baseline CT scans to a slice thickness value of 3 mm using trilinear interpolation. The VFA analysis was then repeated after a five-day wash-out period blinded to the data from the 1.25 mm analyses. The resampling method was tested on an independent set of 30 CT scans for which 1 mm and 3 mm primary reconstructions were made from a single acquisition. Vertebral height ratios were not

significantly different when measured using the 3 mm primary reconstruction compared to using a 3 mm image resampled from the 1 mm reconstruction (p=0.27).

Accuracy of VirtuOst VFA relative to the manual measurements was quantified by the mean difference in vertebral height ratios and by Cohen's kappa for repeatability for a binary no-fracture (Grade 0) versus fracture (Grades 1–3) determination, and for fracture grading on a scale of 0–3. Repeatability of VirtuOst VFA was quantified by kappa for fracture determination and grading, and precision in the vertebral height-ratios on which fracture grades are based was characterized by the root mean square standard deviation in the differences of repeat measurement pairs (SD_{RMS}). Agreement in fracture determination and grading, and differences in vertebral height ratios when using 1.25 mm versus 3 mm CT scan reconstructions were also quantified by these same statistics.

With respect to accuracy, VirtuOst VFA and the manual measurements agreed well for both fracture determination (kappa = 0.94, 95% CI = 0.82–1.06) and grading (kappa = 0.76, 95% CI = 0.60–0.91). There were no significant differences in fracture determination (p = 0.32) or fracture grades (p = 0.32), and the mean difference in the height-ratio between VirtuOst VFA and manual measurements was small compared to the range in height ratios (0.005 vs. 0.17–1.13).

Repeatability of VirtuOst VFA was very good for both fracture determination and fracture grading (**Table 2**). Intra-operator precision of VirtuOst VFA (SD_{RMS} = 0.018) was similar to that of predicate device K103475 (SD_{RMS} = 0.021–0.039). Interoperator precision of height-ratios using VirtuOst VFA (SD_{RMS}=0.023) was also similar to that of the predicate (SD_{RMS} = 0.025–0.048).

Table 2: Repeatability for fracture determination and fracture grades. Results are for intra-operator, interoperator, short-term and combined precision.

	Intra-operator	*Interoperator*	*Short-term*	*Combined*
Fracture Determination: no-fracture (Grade 0) vs. fracture (Grades 1–3)				
kappa	0.94	0.94	0.88	0.82
95% CI	0.82–1.06	0.82–1.06	0.72–1.04	0.62–1.02
p-value	0.32	0.32	1.00	0.56
Fracture Grading (Grades 0–3)				
kappa	0.69	0.72	0.69	0.76
95% CI	0.52–0.87	0.55–0.89	0.53–0.86	0.61–0.92
p-value	0.96	0.57	0.32	0.63

kappa = Cohen's kappa for repeatability; 95% CI = 95% confidence intervals; P-values from Bowker's test

Vertebral height-ratios were smaller on average when measured from 3 mm compared to 1.25 mm slice thickness CT scans (mean = 0.013, 95% CI = 0.003–0.024, p = 0.01), but again the difference was small compared to the range in height-ratios. Agreement in fracture determination (kappa = 0.88, 95% CI = 0.72–1.04) and grading (kappa = 0.66, 95% CI = 0.47–0.84) were still very high between the scans of different slice thickness; and intra-operator precision when slice thickness varied between repeat measurements (SD_{RMS} = 0.034) was still within the range reported by predicate device K103475 when slice thickness was constant.

When one of the repeat analyses was performed on an image with IV contrast enhancement, the height-ratios were larger on average (mean = 0.007; 95% CI = 0.001–0.013, p=0.02). Again the difference was small compared to the range in height-ratios; and intra-operator precision when one repeat measurement was from an enhanced image (SD_{RMS} = 0.020) was similar to precision when both measurements were from unenhanced images.

These data demonstrate that Virtuost VFA is highly accurate and indicate that the precision of VirtuOst VFA is substantially equivalent to that of the predicate; that precision errors are small enough to have no significant effect on fracture determination or grading; and that these conclusion hold for CT scan reconstruction slice thicknesses up to 3 mm with or without IV contrast enhancement.

7) Conclusion

O.N. Diagnostics believes that VirtuOst is substantially equivalent to the predicate devices on the basis of intended use, technological characteristics and the performance data presented.