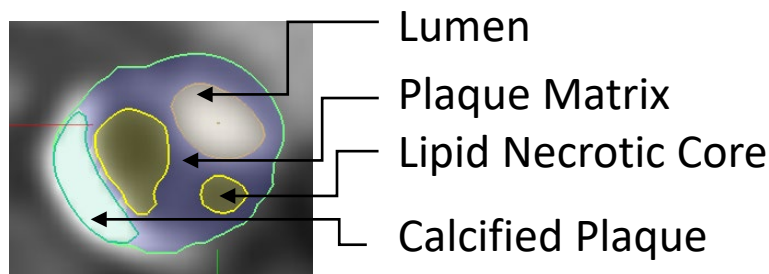


vascuCAP® Clinical Edition is an image analysis tool for evaluating routinely available CT images of arterial vessels now available for clinical use in the United States. vascuCAP® provides multi-dimensional visualization and measurements to aid clinicians in their analysis of arterial anatomy and tissue characteristics. With vascuCAP®, tissue characteristics implicated in high risk atherosclerotic plaque may be quantitatively measured from CT Angiography(CTA) in high correlation with histopathology.

Available anatomical visualization and measurement for clinical decision support include:

- Lumen diameter and wall thickness, shape, and cross-sectional area at 0.5mm intervals along a calculated centerline of one or more chosen arterial segments or multi-segment paths.
- Aggregates of cross sectional data including lumen-wall ratios (stenosis, dilation, plaque burden, and remodeling ratio) segmental and overall volumes by segment or path.
- Length, cross sections and aggregate data of user-defined lesions or other regions of interest.

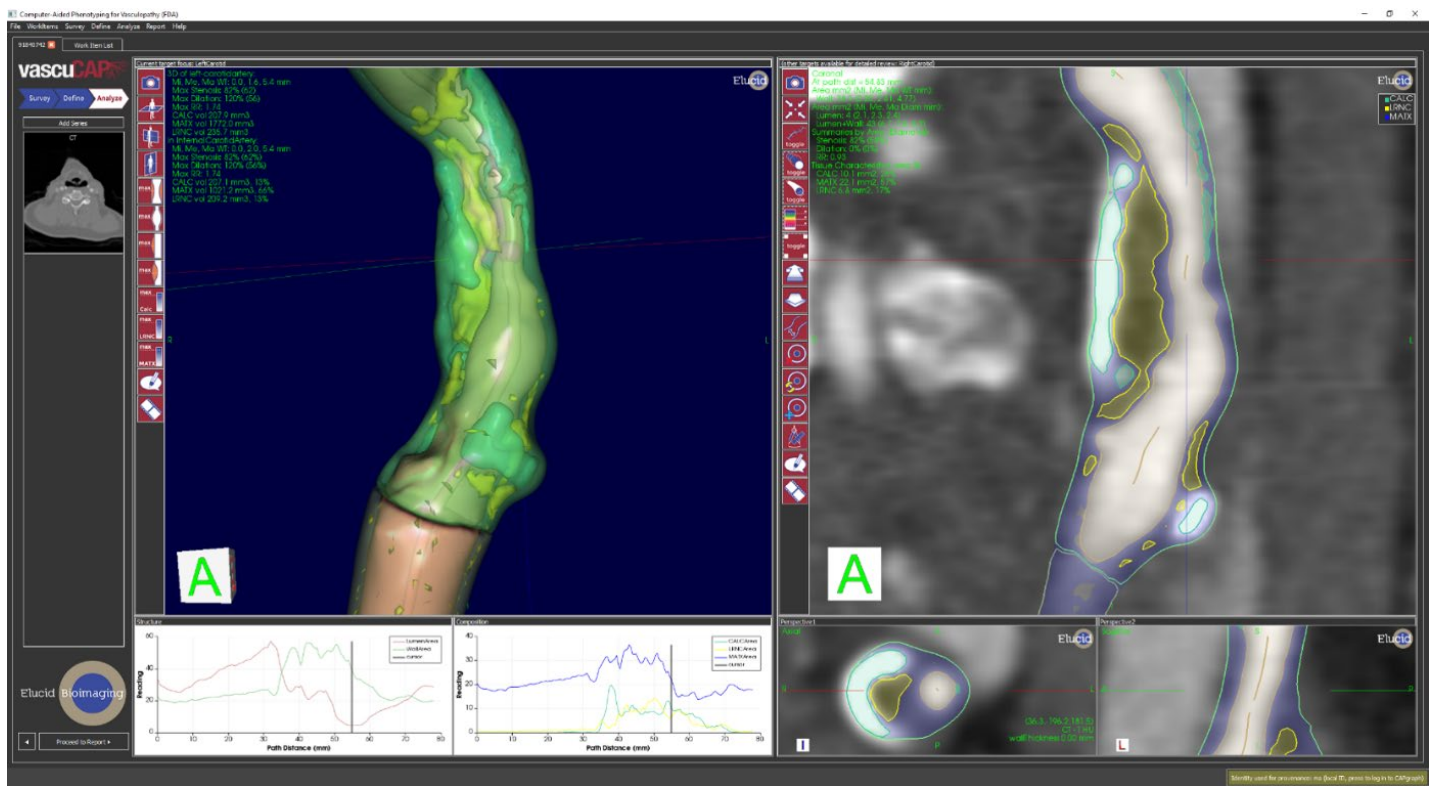


Semi-automatic tissue characterization of vessel wall sub-regions for clinical decision support is available including:

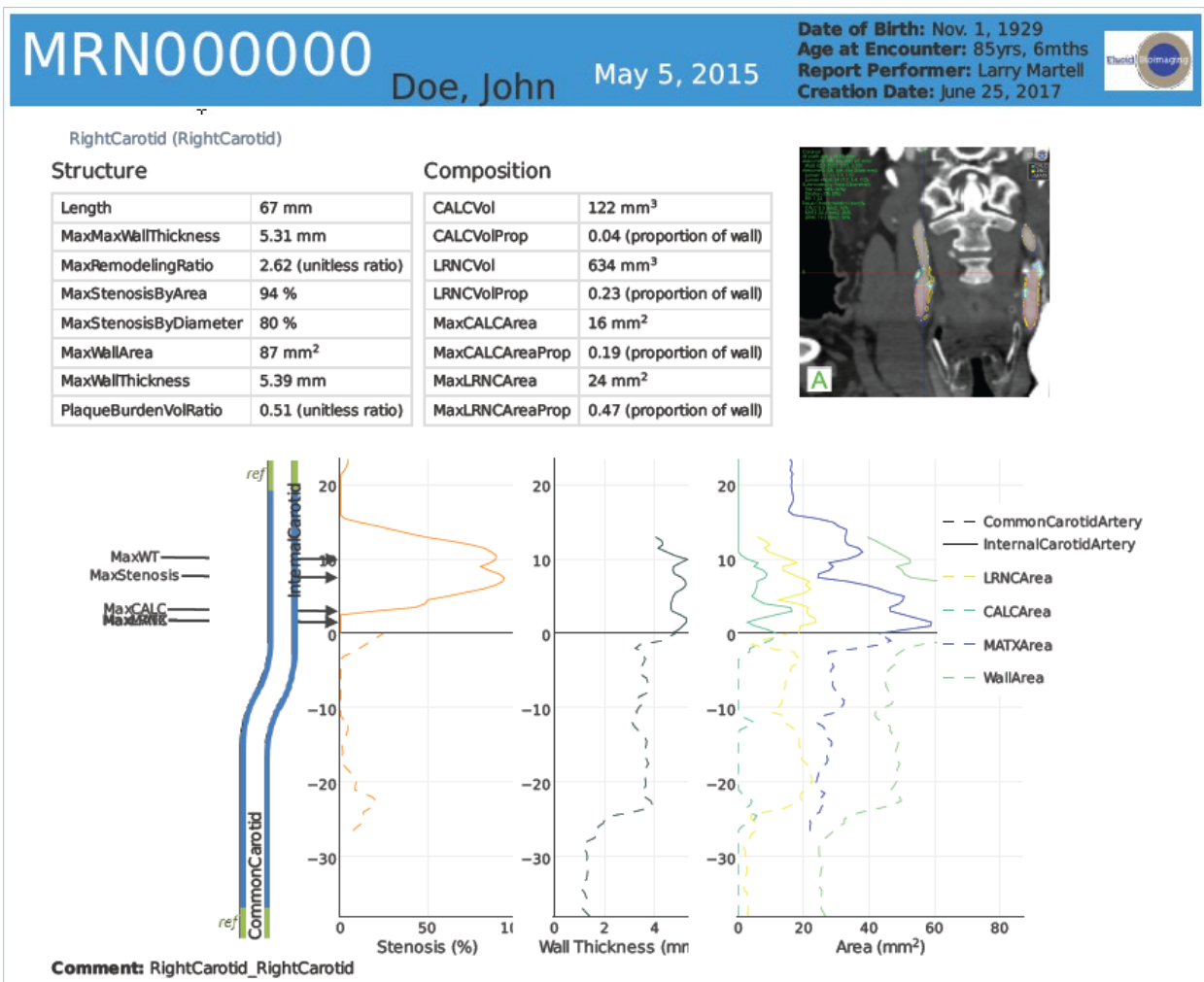
- Measurement of calcified plaque, lipid-rich necrotic core, and matrix areas of interest for each vessel segment or path under user supervision;
 - vascuCAP® is designed to mitigate overestimation of calcification on CTA;
 - vascuCAP® is designed to mitigate underestimation of lipid rich necrotic core on CTA;
- Aggregation of calcified plaque, lipid-rich necrotic core, and matrix area and volume statistics for each vessel, segment, path or user designated lesion (absolute and fractional occupancy);
- Display of calcified plaque, lipid-rich necrotic core, and matrix regions of interest in multiple 2D and 3D formats for clinician to visualize the relative positions of each sub-region to the lumen for treatment planning and outcomes assessment.

vascuCAP® workflow facilitates reporting of the clinician's quantitative findings with supporting visualization and comparison with prior findings using the CAPgraph® informatics solution.

The measurements provided by vascuCAP® are not intended to provide a diagnosis or clinical recommendations. vascuCAP® is intended as a tool to complement standard of care.



Paired with Elucid's CAPgraph[®] informatics solution, vascuCAP[®] is a highly sensitive and highly selective research tool for evaluating vascular disease patients and assessing treatment outcomes.



Performance Data: Validation testing using phantom and clinical images was conducted to address performance qualification of the subject device under typical operating conditions. Clinical images were evaluated using vascuCAP. Objectives evaluated included calculations of anatomic structure (interchangeability with manual measurements as well as inter- and intra-reader variability) and calculations of tissue characteristics (compared to expert annotation by board certified pathologists of histopathologic specimens as well inter- and intra-reader variability). As a result of this testing, the following analytic performance metrics have been established*:

| | | |
|---|--|---|
| Structure | Lumen Area , tested range 0.3 - 290.1mm ² | <i>Bias:</i> 0.81mm ² [0.3, 1.9], <i>Intercept:</i> 0.65mm ² [-0.6, 0.9], <i>Slope:</i> 1.01 [0.9, 1.0], <i>Quadratic term:</i> 0.0 [0.0, 0.0], <i>R²:</i> 0.9987 |
| | Wall Area , tested range 9.4 - 448.6mm ² | <i>Bias:</i> 0.50mm ² [-1.08, 1.29], <i>Intercept:</i> -0.59mm ² [-4.1, 2.8.0], <i>Slope:</i> 1.0 [0.99, 1.04], <i>Quadratic term:</i> 0.0 [0.0, 0.0], <i>R²:</i> 0.9974 |
| | Stenosis** , tested range 33-69% | Vessels ≥5.9mm: <i>Bias:</i> 3.7% [1.29, 4.47], <i>Intercept:</i> 5.99% [-0.81, 9.93], <i>Slope:</i> 0.96 [0.84, 1.1], <i>Quadratic term:</i> -0.01 [-0.02, 0.01], <i>R²:</i> 0.8034 |
| | | Vessels <5.9mm: <i>Bias:</i> 9.3% [2.14, 12.72], <i>Intercept:</i> 34.0% [-2.3, 38.9], <i>Slope:</i> 0.55 [0.42, 1.21], <i>Quadratic term:</i> 0.001 [-0.02, 0.06], <i>R²:</i> 0.9549 |
| | Wall Thickness , tested range 1.0 - 9.0mm | <i>Bias:</i> 0.5mm [0.3, 0.6], <i>Intercept:</i> 0.27mm [-0.1, 0.5], <i>Slope:</i> 1.05 [1.01, 1.1], <i>Quadratic term:</i> -0.008 [-0.02, 0.01], <i>R²:</i> 0.9855 |
| Plaque Burden , tested range 0.4 -1.0 (ratio) | <i>Bias:</i> -0.01 [-0.01, .004], <i>Intercept:</i> 0.01 [-0.1, 0.04], <i>Slope:</i> 0.99 [0.9, 1.1], <i>Quadratic term:</i> 0.03 [-0.1, 0.3], <i>R²:</i> 0.9794 | |
| Composition | Calcified Area , tested range 0.0 - 51.2mm ² | <i>Difference:</i> 0.15mm ² [-0.5, 0.97], <i>Intercept:</i> 0.4mm ² [-0.02, 1.6], <i>Slope:</i> 0.9 [0.6, 1.1], <i>Quadratic term:</i> -0.01 [-0.1, 0.04], <i>R²:</i> 0.875 |
| | LRNC Area , tested range 0.0 - 26.8mm ² | <i>Difference:</i> 0.8mm ² [-0.7, 2.6], <i>Intercept:</i> 1.44mm ² [0.2, 3.4], <i>Slope:</i> 0.8 [0.2, 1.1], <i>Quadratic term:</i> 0.004 [-0.1, 0.3], <i>R²:</i> 0.5222 |
| | Matrix Area , tested range 2.6 - 57.1mm ² | <i>Difference:</i> -1.6mm ² [-3.6, 0.32], <i>Intercept:</i> 2mm ² [-3, 5], <i>Slope:</i> 0.83 [0.7, 1.0], <i>Quadratic term:</i> -0.01 [-0.04, 0.01], <i>R²:</i> 0.7469 |

*brief explanatory notes to help interpret the table:

- Range indicates the smallest and largest true value for the measurand tested.
- Each metric is presented as a point estimate followed by a 95% confidence interval (CI). The CI is computed from the statistics of the observed data. It is acknowledged that wide confidence intervals make the established metric quite uncertain, and in general stem from the number of tested data points and metric specific factors.
- Bias for structural measurands and plaque burden are derived from phantom experiments such that ground truth is assessed using micrometer measurements on anthropomorphic objects. Width of confidence intervals follow from the relative difficulty of each phantom geometry and typical variation experienced across clinically-accepted scanning protocols. The mean tested phantom vessel size is 8.7mm [3.9mm, 23.9mm]. For stenosis, the mean tested vessel size of the vessels ≥5.9mm bin was 5.2mm [3.9mm, 5.9mm], and for the vessels <5.9mm bin was 11.9mm [7.9mm, 23.9mm].
- Systematic difference from histopathology for tissue types is estimated relative to pathologist annotation of ex vivo tissue specimens with paired CTA such that ground truth is assessed based on expert interpretation that the relevant scientific and clinical community relies upon for diagnosis or other specific categorization of the studied tissue. The mean tested specimen vessel size is 7.9mm [3.6mm, 12.9mm]. The tissue specimens are from the carotid artery, and that as a result, may not account for errors due to motion that may be present in imaging of small vessels depending on the use of ECG gating. Width of confidence interval follows from:
 - agreement of pathologists (three independent annotations were used for these results to account for acknowledged discordance in histopathology interpretation),
 - certainty of positioning of annotated sections into 3D radiology volume (four combinations resulting from two unique positioners crossed with two independent radiologist users were used for these results to account for differences in judgment on where the annotated section data applies within the in vivo volume, blinded to vascuCAP results),
 - relative difficulty of physiologic presentation, and
 - typical variation experienced across clinically-accepted scanning protocols.

| | | |
|--------------------|--|--|
| Structure | Lumen Area , range 0.0 - 58.5mm ² | <i>Inter-reader wSD</i> : 3.70mm ² [3.29, 4.23], <i>Intra-reader wSD</i> : 2.01mm ² [1.83, 2.24] |
| | Wall Area , range 0.0 - 106.8mm ² | <i>Inter-reader wSD</i> : 3.05mm ² [2.7, 3.5], <i>Intra-reader wSD</i> : 1.63mm ² [1.48, 1.82] |
| | Stenosis , range 0 - 94.8% | <i>Inter-reader wSD</i> : 11.1% [10.0, 12.5], <i>Intra-reader wSD</i> : 8.2% [7.0, 9.8] |
| | Wall Thickness , range 1.1 - 5.5mm | <i>Inter-reader wSD</i> : 0.7mm [0.59, 0.88], <i>Intra-reader wSD</i> : 0.44mm [0.37, 0.52] |
| | Plaque Burden , range 0.0 - 1.1 (ratio) | <i>Inter-reader wSD</i> : 0.043 [0.042, 0.044], <i>Intra-reader wSD</i> : 0.044 [0.039, 0.048] |
| Composition | Calcified Area , range 0.0 - 44.7mm ² | <i>Inter-reader wSD</i> : 0.72mm ² [0.66, 0.8], <i>Intra-reader wSD</i> : 0.62mm ² [0.56, 0.7] |
| | LRNC Area , range 0.0 - 23.5mm ² | <i>Inter-reader wSD</i> : 1.08mm ² [0.98, 1.19], <i>Intra-reader wSD</i> : 0.50mm ² [0.45, 0.56] |
| | Matrix Area , range 4.03 - 45.1mm ² | <i>Inter-reader wSD</i> : 2.04mm ² [1.9, 2.3], <i>Intra-reader wSD</i> : 1.23mm ² [1.11, 1.37] |

- Inter-reader variability was estimated using two readers selected for typical to low experience reading (C)CTA, trained on the software, operating independently and blinded to each other's results. Confidence intervals follow from the relative difficulty of physiologic presentation, and typical variation experienced across clinically-accepted scanning protocols.
- Intra-reader variability was estimated by one of the readers from the inter-reader study re-reading the same patients but after a "wash-out" period as customary in intra-reader variability studies.

**important note regarding stenosis by diameter: given the reliance of stenosis by diameter as being computed from lumen diameters, and the relative difficulty of accurately estimating lumen diameter as the lumens become appreciably smaller than the finite voxel size, the stenosis may be overestimated. This issue is not unique to vascuCAP but rather a known issue for any interpretation of CTA as lumen size decreases. It is important to follow current clinical training to disregard quantitative calculations of stenosis by diameter from CTA when the lumen is not readily visualized and instead for it to be judged qualitatively. Use of such calculations as %stenosis by area, also available from vascuCAP, mitigates but does not completely avoid this issue.

See User Guide for tables of scanner makes, models, and settings used in the testing as well as patient characteristics of the tested population.