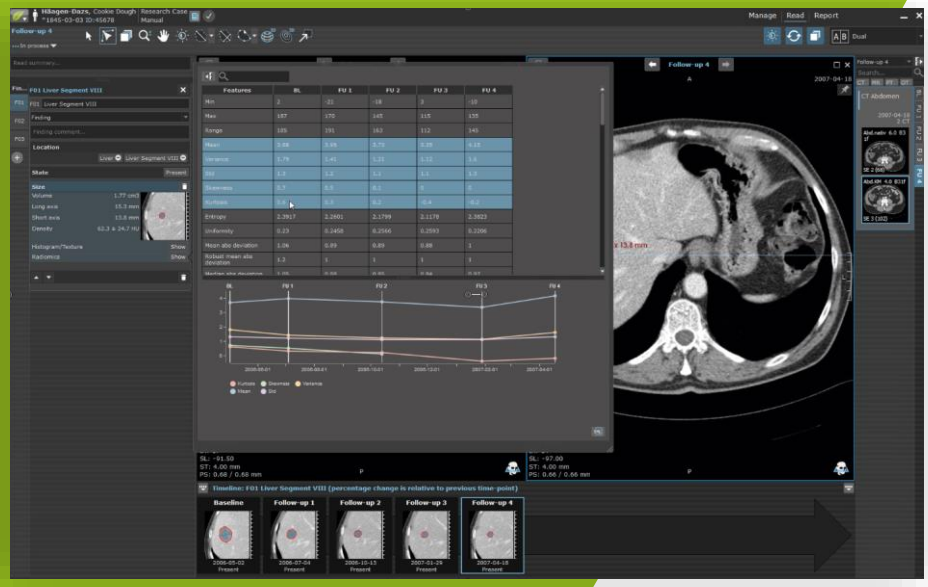
mint®
medical



mint Lesion™

Radiomics Q&A

What is radiomics?

Radiomics is a method to analyze medical images for certain features (radiomic features) that can be quantified. This quantitative image information can then be analyzed and correlated to tumor pathology. Radiomics features include density / intensity, shape, size, and texture amongst others. The quantitative information collected contain first, second, and third order statistical information. When this image data is combined with other patient data, correlations emerge related to diagnosis as well as predicting treatment outcomes. Essentially, taking a standard of care medical image (CT, MRI, PET) and transforming it into data that can be mined for information.

The goal of radiomics is to provide a non-invasive means to improve treatment-related decisions for patient care. While primarily explored as a decision support tool in oncology, radiomics can be applied to virtually any disease indication. Radiomics provides a pathway to enhancing precision medicine by improving the accuracy and efficiency of diagnosis while furthermore improving the precision of therapy selection for positive treatment outcomes.

Is there a key reference that the radiomics features in **mint Lesion™** is based upon?

The radiomics features in **mint Lesion** were developed in accordance with the Image Biomarker Standardisation Initiative (IBSI). This initiative is an independent international collaboration focused on standardizing the extraction of image biomarkers from medical images for the purpose of radiomics. A primary goal of this initiative was the standardization of image biomarker nomenclature and terminology as well as benchmark datasets and benchmark values.

Reference: https://arxiv.org/abs/1612.07003 Zwanenburg, A., Leger, S., Vallières, M., Löck, S., & et al. (2016). **Image biomarker standardisation initiative**. ArXiv, arXiv:1612.07003v6.

What do I need to do in **mint Lesion™** to capture radiomics information?

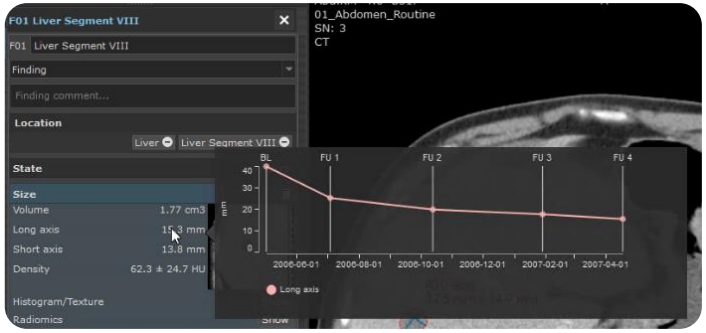
Radiomics features can be applied to standard of care images including CT, MRI and PET. While radiomics features can be extracted from images as part of routine image analysis, any response criteria in **mint Lesion** can also be used to capture radiomics information.

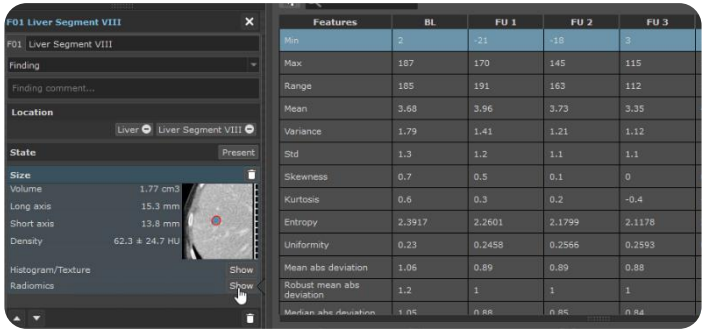
One reason radiomics is a great fit to collect in the background of response assessment evaluation is that large amounts of imaging data are routinely assessed for endpoint evaluation in clinical trials. Radiomics can be collected without interfering with the study trial endpoint analysis while later analyzing the data together with genetic and clinical information. For example, a solid tumor trial can utilize RECIST 1.1 for the endpoint analysis of Progression Free Survival, while also collecting radiomics features in the background without impacting the efficacy evaluation.

In **mint Lesion**, ROI and VOI measurements will also automatically derive the diameter measurements (long and/or short as needed per lesion location type); there is no need to perform an additional measurement for RECIST 1.1.

There are two primary restrictions related to capturing radiomics information:

- Measurements must be performed with either a Region of Interest (Single slice ROI) or Volume of Interest (VOI). Diameter measurements can not be used.
- Modalities are restricted to CT, MRI, and PET.





Incorporating radiomics in response assessment

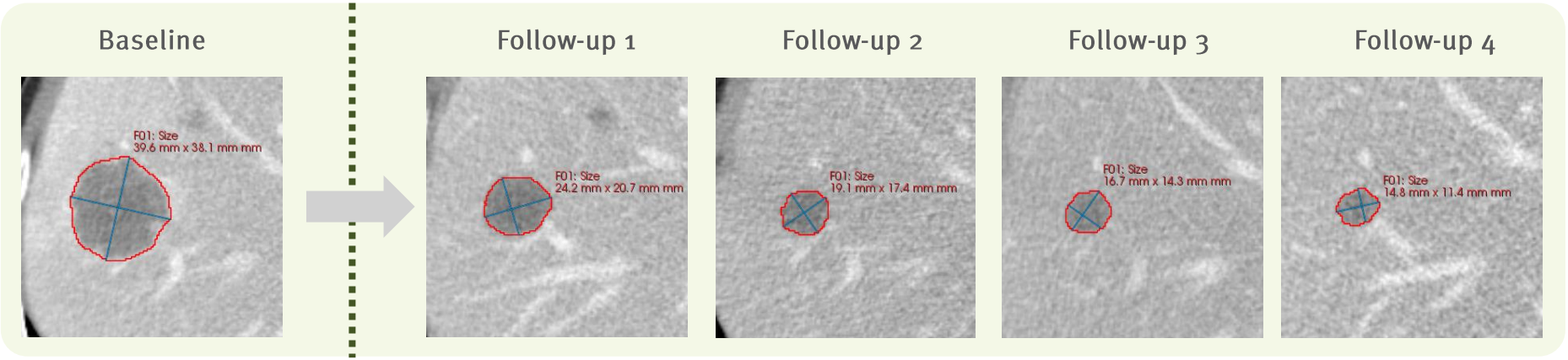
If radiomics will be collected during response assessment (such as RECIST 1.1 evaluation), project planning should consider the following decision points prospectively:

- **Image standardization:** How will images be prospectively standardized to reduce variability in the analysis? This is also important in the reporting of radiomics analysis.

- **Modalities utilized:** Will all data be collected on one modality only (such as CT) or will there be a mixture of modalities? Multi-modality data can reduce overall sample size.

- **Measurement tool utilized:** Will a ROI or VOI be used to annotate lesions for measurement?

- **Measured sites:** Which lesions will be measured during the analysis? For example, in a RECIST 1.1 study, only Target Lesions are typically measured but it may be meaningful to also collect measurements on Non-Targets and New Lesions.



What radiomics features does **mint Lesion™** extract?

mint Lesion currently provides first and second order texture features.

- First-order being those features which use only the values of individual pixels in the image and do not relate to other image pixels. Thus spatial relationship is not considered. Examples are mean/median/maximum/skewness/kurtosis of the identified pixel values.
- Second-order being those features that take into consideration neighboring pixel values in an image. These are features defined by a statistical relationship between pixels.

Morphology	Intensity-based	Histogram-based (1st order texture)	GLCM-based (Gray-level co-occurrence matrix) (2nd order texture)
Volume Area	Min Max Mean Standard deviation	Min Max Mean Standard deviation Skewness Kurtosis Uniformity Entropy Mean absolute deviation Robust mean absolute deviation Median absolute deviation Coefficient variation Quartile coefficient dispersion Range Interquantile range P10th / p25th / p50th / p75th / p90th / p100th Minimum histogram gradient Minimum histogram gradient intensity Maximum histogram gradient Maximum histogram gradient intensity	Joint maximum / Joint average Standard deviation Joint variance Joint entropy Difference average Difference variance Difference entropy Sum of averages Sum of variance Sum of entropy Angular second moment Contrast Dissimilarity Inverse difference Inverse difference normalized Inverse difference moment Inverse diff. moment normalized Inverse variance Correlation Auto correlation Cluster shade Cluster prominence Cluster tendency Information correlation 1 / 2

Does **mint Lesion™** have any limitations with regard to radiomics?

mint Lesion implements only GLCM based texture features.
The GLRLM, GLSZM, GLDZM, NGDTM and NGLDM are currently not supported.

How is data exported for radiomics features?

Radiomics features can be exported to XML or CSV.

Trial / Subject cohort data can be exported with multiple configuration filters applied.

Additionally, a Radiomics Display Widget in the Read Screen can be used to change configurations on the fly and export the features on a subject / case level. This feature is important for detailed radiomic feature investigation and outlier analysis as well as optimizing configuration application on a Trial / Subject Cohort level.

See further information in dedicated section on image post-processing and standardization.

Can measurement annotations performed on DICOM images be exported?

In addition to data exports, the images from **mint Lesion** support all data representations common in industry and research:

- **NRRD / NIFTI** - file based export that can easily be imported into pyRadiomics, Tensorflow, pyTorch, etc.
- **DICOM RT Struct** - DICOM based export with related advantages in data portability, archiving, as well as support by radiotherapy planning systems, etc.
- **DICOM Segmentation Objects** - DICOM based export with advantages and oftentimes used by researchers and some biopsy device manufacturers
- **DICOM SR** - DICOM based for (bi-)diameter measurements

Are there reporting guidelines for radiomics?

The Image Biomarker Standardisation Initiative suggests guidelines for consistent reporting of both image processing and feature calculations.

These reporting guidelines include the following suggested details:

- **General** - Image acquisition, reconstruction, approach (2D or 3D), process workflow, software (**mint Lesion**), data availability
- **Data Conversion** - Procedures for how data converted from reconstructed image data and any associated algorithms.
- **Image Post-Acquisition Processing** - Procedure for post-processing steps and parameters and any associated algorithms.
- **Segmentation** - ROI delineation (Targets, Non-Targets, etc.), procedure (manually or auto-segmentation)
- **Interpolation** - Voxel dimensions, image interpolation method, image intensity rounding, ROI interpolation method, ROI partial volume
- **Re-Segmentation** - ROI mask criteria
- **Discretization** - Discretization method, discretization parameters
- **Feature Calculation** - Feature set, feature parameters, standardization

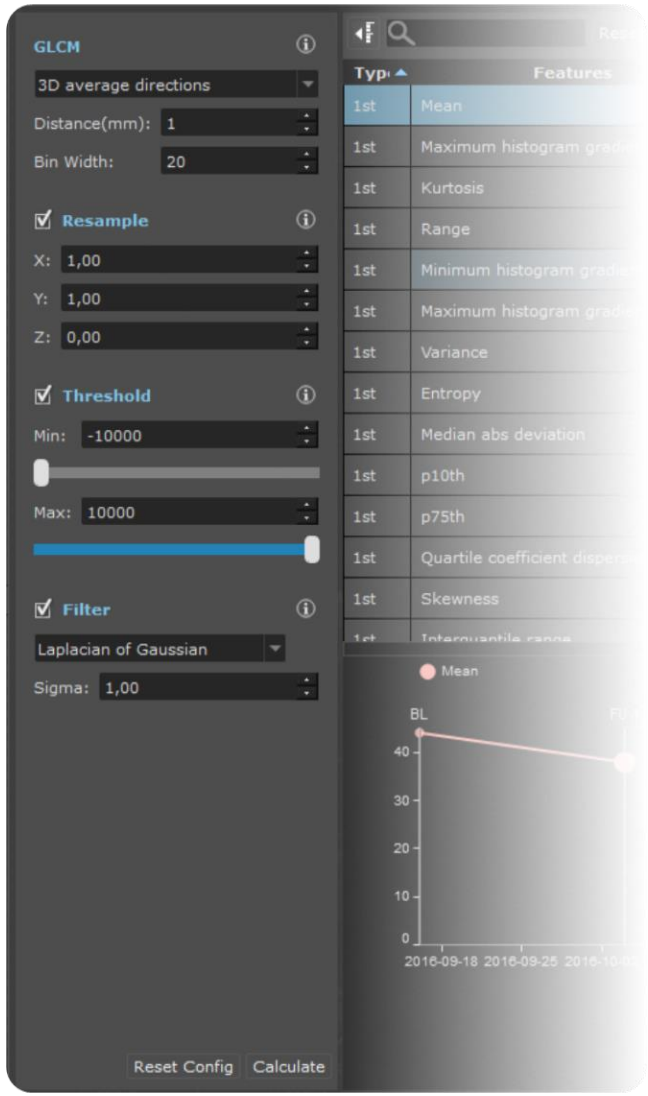
How did Mint Medical validate the radiomics features?

mint Lesion validated the radiomics features against the benchmark data set by the ISBI (arXiv:1612.07003). The **mint Lesion** reported results were compared to the benchmark published values by ISBI and the calculated features corresponded to the IBSI results.

Can Mint Medical provide the mint Lesion™ methods for calculation of features?

The IBSI publication is extensive and provides all the details about the calculation of radiomics features that **mint Lesion** adheres to.

Image post-processing and standardization - **mint Lesion™** radiomics configurations



Laplacian of Gausian (LoG) filter

The Laplacian is a 2D filter applied to the medical image as pre-processing step. The Laplacian highlights regions of rapid intensity change and is therefore often used for edge detection. It is applied after smoothing the image with something approximating a Gaussian smoothing filter in order to reduce its sensitivity to noise. This is combined in the Laplacian of Gaussian filter. This can be enabled by configuration and the only parameter to be specified is the standard deviation (sigma) in order to define the extent of smoothing.

Threshold filter

The threshold filter can be used to limit the calculation of radiomics features to a specific range of intensity values. This is particularly interesting for CT images by targeting specific density values. The lower and upper bound can be used to set the interval of values to be used for radiomics derivation.

Resampling

Resampling helps to account for different spatial resolutions of medical images, in most cases a different slice spacing compared to the spacing within the image slices itself. Resampling will recalculate the medical image and generate a new image with the desired spatial resolution. This happens either by upsampling or downsampling the image intensity values by tri-linear interpolation (interpolation across image slices). The x- and y-spacing values are used to set the new resolution of the in-plane directions. The z-value is applied to the resolution between image slices (planes). A "0" value means that the resolution is not changed in the respective direction.

Discretization

When calculating histograms (for 1st order) or GLCMs (for 2nd order) the binning method describes how intensities are grouped for frequency analysis.

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Please contact Mint Medical in case of any questions
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