Software Version 5.0.x
eIFU Version 5.0.x.4
eIFU release date: 2017-05-19

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Regulatory:

CE_{0086} Dynamika is a class IIa medical device within the scope of directive 93/42/EEC

FDA   Dynamika has 510(k) clearance under the following number: K161601

Used symbols:

i   **Note:**
This symbol indicates special information for easier product operation or it provides other important information.

⚠   **Caution:**
This warning symbol indicates important safety related information, like warnings and precautions which cannot be placed on the medical device itself.

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Support, Complaints and Feedback

If you are unable to find the help you need in this user manual, if you have found a problem with the software or if you need a new feature that has not yet been implemented in Dynamika, please contact us using the contact details on the front page of the manual. For your convenience, an accident form and a general reporting form may be found below.

Accident Reporting Form

Date:	

	From:	To:
Name:		Customer Support Manager
Company Name:		Image Analysis Ltd
Address 1:		QABC Minster House
Address 2:		272-274 Vauxhall Bridge Road
Address 3:		London
County/Region:		
Country:		United Kingdom
Post/ZIP Code:		SW1V 1BA
Telephone:		+44 (0) 7413022053
Email:		support@imageanalysisgroup.com

Product Name:	Dynamika Enterprise
Release:	
Computer Hardware:	

Incident Date:	
Severity:	

Description

General Reporting Form

Date:	

	From:	To:
Name:		Customer Support Manager
Company Name:		Image Analysis Ltd
Address 1:		QABC Minster House
Address 2:		272-274 Vauxhall Bridge Road
Address 3:		London
County/Region:		
Country:		United Kingdom
Post/ZIP Code:		SW1V 1BA
Telephone:		+44 (0) 7413022053
Email:		support@imageanalysisgroup.com

Product Name:	Dynamika Enterprise
Release:	
Computer Hardware:	

Urgency:	

Description

Intended Use / Indications for Use

Dynamika Version 5.0 is an image processing software package to be used by trained medical professionals with a level of medical expertise (including physicians, radiographers and radiology technicians). The software runs on a standard off-the-shelf workstation and can be used to perform image viewing, processing and analysis of medical images. Data and images are acquired through DICOM compliant imaging devices and modalities.

Dynamika Version 5.0 provides both viewing and analysis capabilities of dynamic imaging datasets acquired with MRI.

Dynamika Version 5.0 is used for the visualization, analysis and reporting of dynamic MRI data, showing the properties of changes in contrast over time.

The package may be used to calculate permeability parameters related to the leakage of injected contrast material from intravascular to extracellular space. Parametric maps may be overlaid onto the original image for interpretation.

Dynamika Version 5.0 is intended to be used within hospitals and medical clinics. It is licensed and not intended for general public use.

Limitations

The software is not intended for primary interpretation of digital mammography images.

Patient management decisions are the responsibility of the licensed physician and should not be made solely on the results of the Dynamika analysis.

Essential Safety Information

This document is intended to assist users in the safe and effective operation (as per IEC 60601-1, Ed. 3: Medical electrical equipment - Part 1: General requirements for basic safety and essential performance) of the DYNAMIKA software ('Equipment').

The equipment is intended to be installed, used and operated only in accordance with the safety procedures given within this manual for the purpose for which it was designed. The intended use is given above.

Use of the equipment for purposes other than those intended and expressly stated by the manufacturer, as well as incorrect use or operation, may relieve the manufacturer or his agent from all or some of the responsibility for resultant non-compliance, damage or injury.

Installation, use and operation of Image Analysis Ltd. product is subject to the law in the jurisdictions in which the equipment is being used.

Users shall only install, use and operate the equipment in such ways that do not conflict with applicable laws or regulations which have the force of law.

While Image Analysis Ltd. is committed to data security by deploying Dynamika enterprise edition using only cloud-based service providers with state-of-the-art data security and data encryption technology, it is the responsibility of the user to manage access to any local

installation of the Equipment as DICOM data in the local data storage container is unencrypted for such instances. Dynamika is compatible with DICOM standard.

Every effort is made to ensure all Image Analysis software is virus free. It is recommended that all computers used to run or access Dynamika have up to date virus protection.

This manual is written for a skilled physician who is a trained diagnostic MRI clinical personnel. The use of the equipment is not intended to replace judgements of experienced clinical personnel. The user includes the body with authority over the equipment and those persons who actually handle the equipment. Nothing stated in this manual reduces user's professional responsibilities for sound judgment and best practice.

Important Safety Directions

Image Analysis Ltd. products are designed to meet stringent safety standards. All medical devices require proper installation, operation, and maintenance (particularly with regard to safety).

Before attempting to work with this equipment, the user should

- ✓ Read, understand, note and strictly observe all Cautions and Safety markings on the equipment.

- ✓ Strictly follow all Cautions and Notes throughout this manual to help ensure the safety of users and patients.

- ✓ Read and understand the manual.

- ✓ Read and understand any Installation Instructions and Release Notes delivered with the software.

The documentation shall be kept with the system for easy reference. The most extensive configuration is described within this manual, including the maximum number of options and accessories. Not every function, option, or accessory described may have been purchased or licensed on a particular piece of equipment.

Image Analysis Ltd. does not guarantee the quality, the accuracy, or the legality of the MR images based on which the software calculates parameters. The user must, therefore, use caution when using the software.

CAUTION

Due to the use of colour to graphically display the results of statistical calculations throughout the software it is required that the user's level of sight enables them to distinguish red, green and blue colours.

Training

The user of the equipment shall have received adequate training on its safe and effective use before attempting to work with it. Training requirements may vary from country to country. The user shall make sure that training is received in accordance with local laws or regulations that have the force of law. Information on training is available from your local Image Analysis Ltd representative or can be received by contacting Image Analysis support team via email or phone given above.

Training materials available for the use of Dynamika include:

- eIFU (mandatory) - this document
- Webinars
- Live training
- Online tutorials

CAUTION

To ensure safe usage of DYNAMIKA and interpretation of any parameters obtained from the software should be used by a skilled physician. When interpreted by a trained, licensed physician, this device may provide clinically relevant information that may be useful in screening,, intervention planning and monitoring. The use of DYNAMIKA is not intended to replace a diagnosis by a licensed, skilled physician and does not constitute medical advice or diagnosis obtained from the physician.

Product Maintenance

This product is supplied by Image Analysis Ltd. and is supported under Image Analysis Ltd standard support program. If you have any questions about this product, please contact your local representative or email your question directly to support@imageanalysisgroup.com. Image Analysis Ltd. may at its sole discretion, address issues and bugs reported, but responses are provided "AS IS", with no warranty, as stated above and are not guaranteed to address the issue or bug. The product is maintained by Image Analysis Ltd. development team and the user will be advised via email when the next release of the software is available.

⚠️**CAUTION**

Changes to the equipment outside of the Software Installation Package carried out by persons without appropriate qualifications and training may lead to malfunctioning of the software as well as making the warranty void.

Environmental Protection

Please note that at the product recall request, the user shall follow the instructions on how to un-install the software or contact Image Analysis Ltd. to arrange un-installation. No environmental damage should occur when instructions are followed.

Disclaimer

Image Analysis Ltd assumes no liability for use of this document if any unauthorized changes to the content or format have been made. Every care has been taken to ensure the accuracy of the information in this document. However, Image Analysis assumes no responsibility or liability for errors, inaccuracies, or omissions that may appear in this document. This manual is provided without warranty of any kind, implied or expressed, including, but not limited to, the implied warranties of merchantability and fitness for a particular purpose.

⚠️**CAUTION**

Image Analysis Ltd. reserves the right to change the equipment without further notice to improve reliability, function or design. Image Analysis reserves the right to modify the design, packaging, specifications and options described herein without prior notice. Please contact Image Analysis representative for the most current information.

⚠ **CAUTION**

The information in this document contains general technical descriptions of specifications and options as well as standard and optional features which do not always have to be present in individual cases.

⚠ **CAUTION**

Any technical data contained in this document may vary within defined tolerances. Original images always lose a certain amount of detail when reproduced.

⚠ **CAUTION**

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⚠ **CAUTION**

Dynamika does not guarantee the quality, accuracy or legality of the images based on which the software calculates the parameters.

⚠ **CAUTION**

The user may not publish data or information that compares performance of the SOFTWARE with that written by others without prior agreement with Image Analysis Ltd.

User Licence Conditions

⚠️**CAUTION**

Carefully read the terms and conditions below before using the software. Use of the software implies acceptance of the terms and conditions stated below.

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USER LICENSE AND LIMITATIONS

With this licence, Image Analysis Ltd grants the final user the right to use the software on one computer only, unless specified otherwise. In any event the user may not make unauthorized copies and/or reproductions of the SOFTWARE or parts of the latter, including the documentation enclosed. On the basis of the above, and given that the SOFTWARE is not protected against copying, one copy only may be made for safety purposes (backup). The user may not hire, lease or loan out the SOFTWARE, but may transfer rights permanently according to the conditions herein, provided that all copies of the SOFTWARE and written material are transferred and the new owner accepts all conditions. Transfer of the product must always include the latest update and all previous versions. The user may not convert, decode, disassemble or modify the SOFTWARE. The user may not remove, tamper with or alter the copyrights, trademarks of other proprietary rights affixed or enclosed in the SOFTWARE. The user may not publish data or information that compares performance of the said SOFTWARE with that written by others.

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General Release Notes

Electronic Instructions for Use

- The user manual (this document) is available in the application by clicking the help button ?▾ on any page after login and selecting "Download user guide in PDF" or on the web http://www.imageanalysisgroup.com/dynamika-online-resources

Data Security

- Dynamika's cloud-based edition is only deployed on service providers with state-of-the-art data security and data encryption technology
- It is the responsibility of the user to manage access to any local installation of Dynamika as DICOM data in the local data storage container is unencrypted. It is recommended to use hard-drive encryption.

Virus Protection

- Every effort is made to ensure all Image Analysis software is virus free
- It is recommended that all computers used to run or access Dynamika Enterprise have up to date virus protection

Licences

- To receive licences to run the software please contact support at support@imageanalysisgroup.com

System Requirements

- Dynamika Enterprise™ is a web based application that can be installed on a server and accessed from client computers via a web browser. It is possible to install the server components on a personal computer and use Dynamika as a 'Workstation'.
- Installation of the server side software is to be conducted by qualified, trained Image Analysis IT personnel, only.

Server requirements

- Operating System: Linux/Windows Server 2003 (Ubuntu Linux preferred)
- Processor: minimum Dual Core (8 recommended)
- RAM: minimum 4GB (8-16GB recommended)
- Disk: Enough to store all images, minimum 50GB

Client requirements

- Processor: Intel Core i3 (Intel Core i7 recommended) or comparable
- RAM: minimum 4GB
- Minimum screen resolution: 1024x768

Browser Requirements

- Chrome v50 or later – recommended using latest stable release
- Firefox v45 or later
- Safari v9 or later

PC/MAC requirements (as Workstation)

- PC Operating System: Windows 7, 8.x, 10,
  Linux Ubuntu 12 or later, Debian 7 or later
- MAC Operating System: MAC OS 10.9 or later
- Processor: minimum Intel Core i3 dual-core (Intel Core i7 with 8 cores recommended) or comparable
- RAM: minimum 4GB (8-16GB recommended)
- Disk: Enough to store all images, minimum 50GB

Thank you for using DYNAMIKA!

We look forward to hearing your feedback and suggestions

Dynamika, Dynamika Enterprise, Dynamika Workstation and Dynamika-RA are trademarks of Image Analysis Ltd ©2009-2017

Instructions for Use

1.   Introduction

Dynamika is a cloud based software platform providing data management and visualisation, quantitative biomarkers and automated reporting for advanced biomedical imaging applications.

Dynamika can be used on any computer connected to the internet. All images, reports and other associated data uploaded to and processed in Dynamika are stored in the cloud and can be accessed securely from anywhere. Dynamika also provides HIPAA compliant patient anonymization functionality to remove all patient sensitive information from the DICOM headers of the medical images before upload, such that no patient identification information ever leaves the site where the data is uploaded.
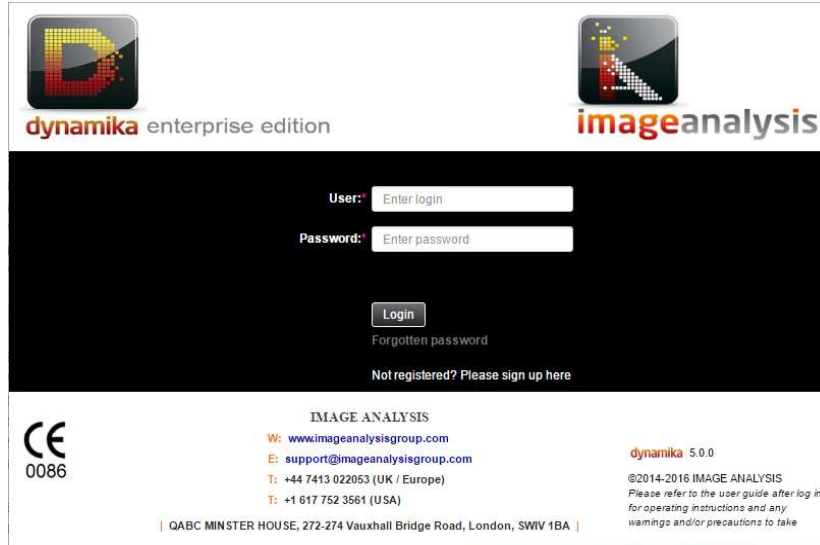
i	Patient sensitive information that is contained directly in the images, such as "burned-in" patient information in secondary captures or patient features visible through 3D rendering techniques, are not removed or masked by the software.

There are several different modules to Dynamika, which will be broken down into separate sections in the Instructions for Use as follows:

The starting point of a Dynamika session is the landing page:

Please enter the username and password you have been assigned and press login, your Dynamika session will begin. If you have forgotten your password, press the "Forgotten password" link and you will be sent a new password to your designated email.

If you are new to Dynamika and do not have a username or password assigned, please follow the "Not registered?" link or email support@imageanalysisgroup.com to get started.
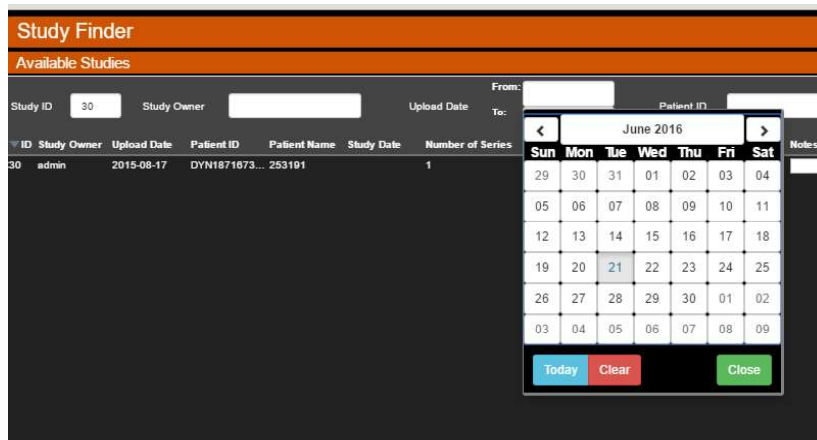
2. Data management and general visualisation

The first view encountered in Dynamika is the *Study Finder*. Here you can browse studies that belong to you or have been shared with you:

The top pane, *Available Studies*, shows all the data you have uploaded, or that has been shared with you by other people, you can scroll through these studies using the mouse wheel, or use the slider at the far right of the screen.

A helpful feature is the filters at the top of the screen which allow you to filter by selected fields or date ranges, this will reduce the list to match your input specifications:

2.1 Data upload

Dynamika supports data upload from three different sources. The recommended option is to create a zip file containing one or more studies and to upload the zip file using the "Upload Studies as Compressed Archive" button.

If desired, one can also upload individual DICOM files via "Upload Studies as Files" or retrieve data from a connected PACS if configured.

The upload process allows you to run one of the following algorithms as an automatic pre-processing step:

- Anonymise DICOMs before upload

- Run patient motion correction automatically (see Section 3 Patient motion correction)

- Run parametric maps calculation automatically (see Section 4 Parametric Maps)

If the anonymization option is enabled, the software will offer you to download an Anonymisation Map in the upload dialogue. Please make sure to download such map <u>after</u> the upload has completed (to ensure that the map contains all series information), but <u>before</u> closing the upload dialogue (as this information cannot be recovered at a later point). The format of the map and how to open it with Microsoft Excel is detailed in Appendix A.

2.2   Data selection

The *Available Studies* pane lists all studies that have been uploaded, retrieved via PACS, or shared with you. The *Selected Studies* pane beneath shows all the studies you have chosen to work with. To select a study click on the row in the *Available Studies* pane and drag it into the *Selected Studies* pane. Alternatively, you can double click, or press the Add button.

If you wish do delete studies, or series within studies, drag the studies you wish to manage into the *Selected Studies* pane and press the "Manage Studies" button:
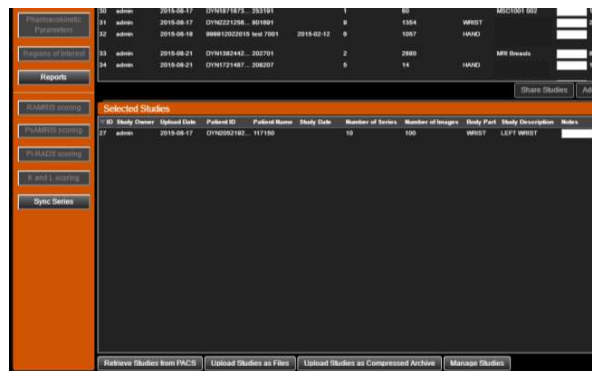
Here you can delete or restore series within a study. To delete the entire study, select all series and press "Delete Series". If you select the "Deleted series" checkbox you will be able to view any deleted series in the currently selected study; you can restore deleted series into the study by pressing "Restore Series".
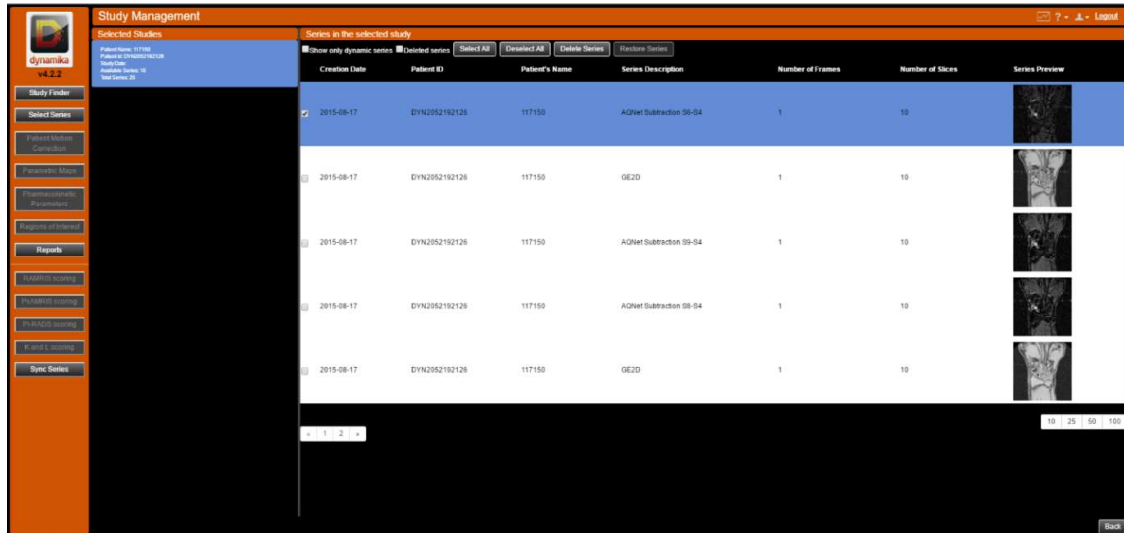
2.3 Data visualisation

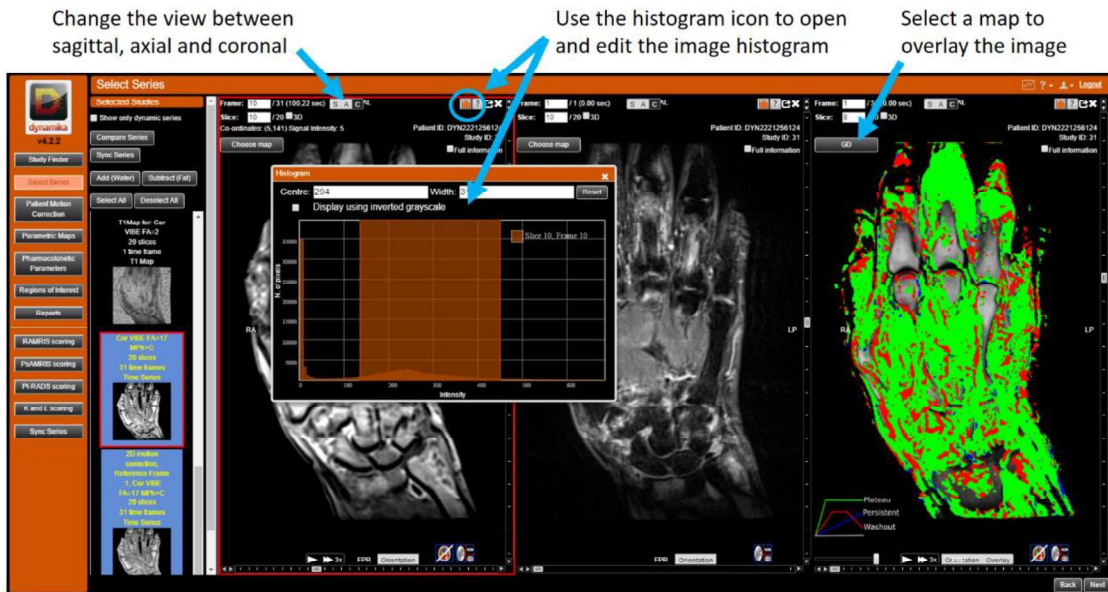Once you have chosen the studies you want to work with in your Dynamika session, you can move to the *Select Series* screen to view your data. You can reach this screen by either pressing the "Next" button in the lower right corner of the screen, which will navigate you through the suggested workflow, or you can press the button labelled Select Series on the left side of the screen.

The left hand scroll menu contains thumbnails of all the series present in the studies you currently have open. Left click on a study to open it in a new image portlet in the viewing pane. The currently selected series is identifiable by a red border around the image portlet and also around the series entry in the left hand scroll menu. If multiple studies are being viewed in the *Select Series* screen, the series that is highlighted with a red border is the one that will be viewed (and analysed) in subsequent pages of the software. To change which series is selected, simply click in the image portlet of the series you wish to select, and the red border will indicate the newly selected series. You may open and browse numerous studies in the *Select Series* view.

Change the view between sagittal, axial and coronal

Use the histogram icon to open and edit the image histogram

Select a map to overlay the image

2.3.1 Image portlet controls
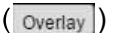
The image portlet provides various controls for image navigation and manipulation as well as various display options. A *Support space* can be accessed by pressing the "?" button (?) in the top right of the image portlet.

Navigation controls:

- To change the slice viewed you can use the scroll bar on the right hand edge of the image portlet, alternatively scroll using the mouse wheel, or manually enter a slice number in the appropriate text box in the top left corner of the portlet.
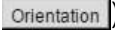
- To change the time frame viewed you can use the scroll bar on the bottom edge of the image portlet, alternatively scroll with Alt + mouse wheel, or manually enter a frame number in the text box in the top left corner of the portlet (dynamic series only).
    - You can play a temporal movie of the time frames in the series by pressing the "Play" button (▶ ▶1x) at the bottom of the image portlet. By pressing the "Increase Speed" button, you can cycle through speeds of playback (1x, 2x, 3x, or 4x). The "Play" button changes to a "Stop" button when a movie is being played.

- To zoom in/out of the image use the up/down arrow keys. Note that zoom is centred upon the cursor position. To reset, right mouse button click in the image portlet and press "Reset Pan and Zoom".

- To pan the image up/down/left/right use Ctrl + arrow keys. To reset, right mouse button click in the image portlet and press "Reset Pan and Zoom".

- To change the orientation of the displayed image to either Sagittal, Axial or Coronal press the appropriate button from the controls towards the top left of the image portlet (S A C).

- Orientations can be cached by pressing the "Orientation" button (Orientation) at the bottom of the image portlet. This allows for faster scrolling between slices and timeframes.

Manipulation controls:

- To change the contrast/brightness of the displayed image, hold down the right mouse button and drag up/down/left/right:
    - Dragging right/left will increase/decrease the Width of the histogram meaning pixels with a greater/smaller range of intensities are displayed.
    - Dragging up/down will decrease/increase the Centre of the histogram meaning pixels with lower/higher intensities are displayed.
    - To reset, right mouse button click in the image portlet and press "Reset Brightness / Contrast"

- The histogram can be accessed by pressing the Histogram icon ( )in the top right of the image portlet, allowing Centre and Width values to be entered manually or reset. You can also invert the grayscale of the image by selecting the "Display using inverted grayscale" checkbox.

- A parametric, pharmacokinetic or statistical map, if calculated (see section 4 Parametric Maps and 5 Pharmacokinetic Parameters), can be overlaid on the image:
    - Press the "Choose map" button (Choose map) and select a map from the drop-down menu on the top-left of the image portlet.
    - Pixel intensity (or opacity) of the parametric map can be changed using the slider on the bottom left of the image portlet, alternatively press the M key to switch between full and no intensity.
    - Overlays can be cached by pressing the "Overlay" button (Overlay) at the bottom of the image portlet. This allows for faster scrolling between slices and timeframes when maps are displayed.

- The image portlet can be opened in full screen mode by pressing the full screen mode icon ( ) in the top right corner of the image portlet. This opens in a new tab in the web browser.

Information display options:

- Information about the series can be displayed by selecting the "Full information" checkbox in the top right of the image portlet, beneath the Patient ID and Study ID. This displays Patient Name, Study Date, Institution, Modality Manufacturer, Manufacturer's Model Name, TR value (ms), TE value (ms), Magnetic field strength, Slice Thickness, Upload Date, Image.

- Full DICOM headers can be viewed by right mouse button clicking in the image portlet, then clicking "Show DICOM headers". These can be filtered by Tag Description by searching in the text box at the top of the *DICOM Header View* portlet.

2.4 Further view options

Once you have selected the studies you wish to view in the *Select Studies* screen, Dynamika offers extra view options for more detailed visual comparison of series.

Compare Series screen:

The *Compare Series* screen offers comprehensive slice statistics alongside each series. It also offers signal-time curve visualisation for dynamic series in the top left pane.

Sync Series screen:

The *Sync Series* screen offers spatial synchronisation of series for advanced visualisation and localisation.

Series can be dragged and dropped into portlets from series list

Slice locators show slice position of alternate orientations
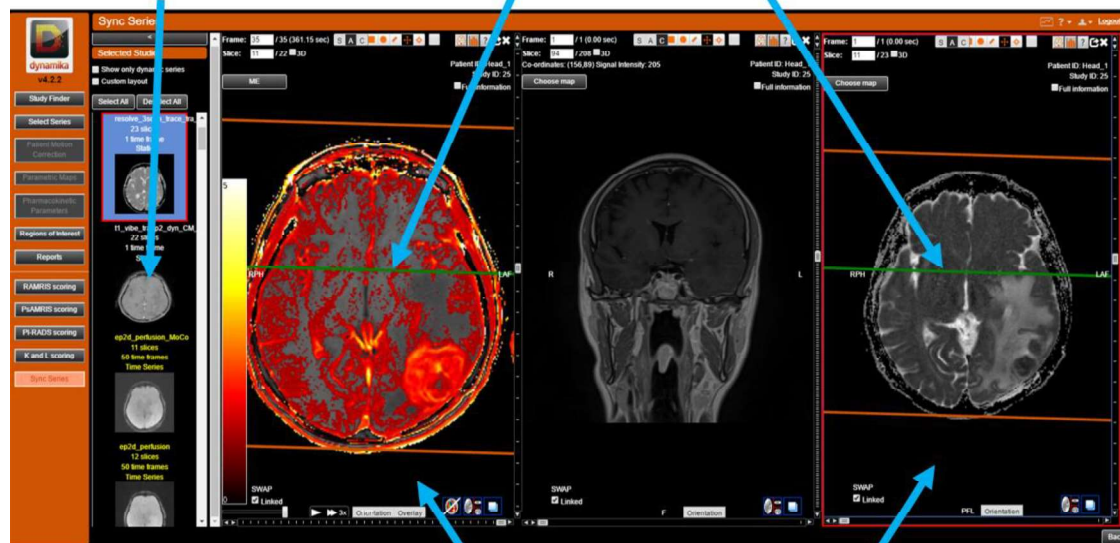
Series in same orientation scroll in sync

Series opened together in the *Sync Series* screen will spatially synchronise such that they can be scrolled in conjunction in the same orientation. Series visualised in different orientations will produce linear locators to define the current slice location in portlets with alternate orientations (green locator), and the boundaries of the volume (orange locators).

Multiplanar Reconstruction screen:
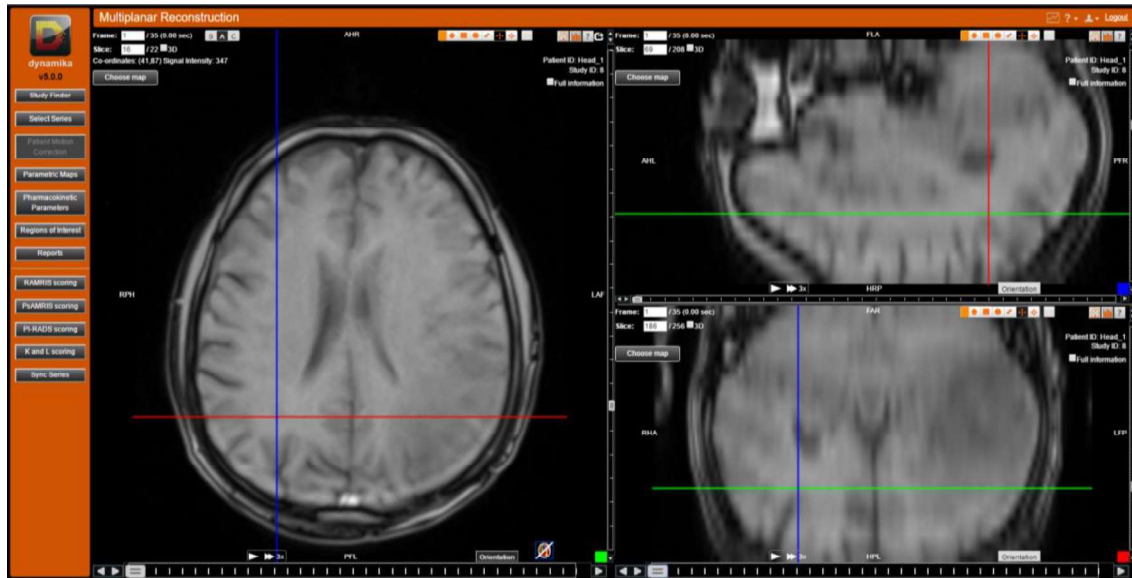
The *Multiplanar Reconstruction* screen is accessed by pressing the "Multiplanar Reconstruction" button ( ). The *Multiplanar Reconstruction* screen can be accessed from any image portlet and is opened in a new tab in the browser. Here you can view the images in a series in all three orientations simultaneously. The three image portlets are synchronised with moving reference lines that indicate the position of the other orientations on the image.

Compare Parametric Maps screen:
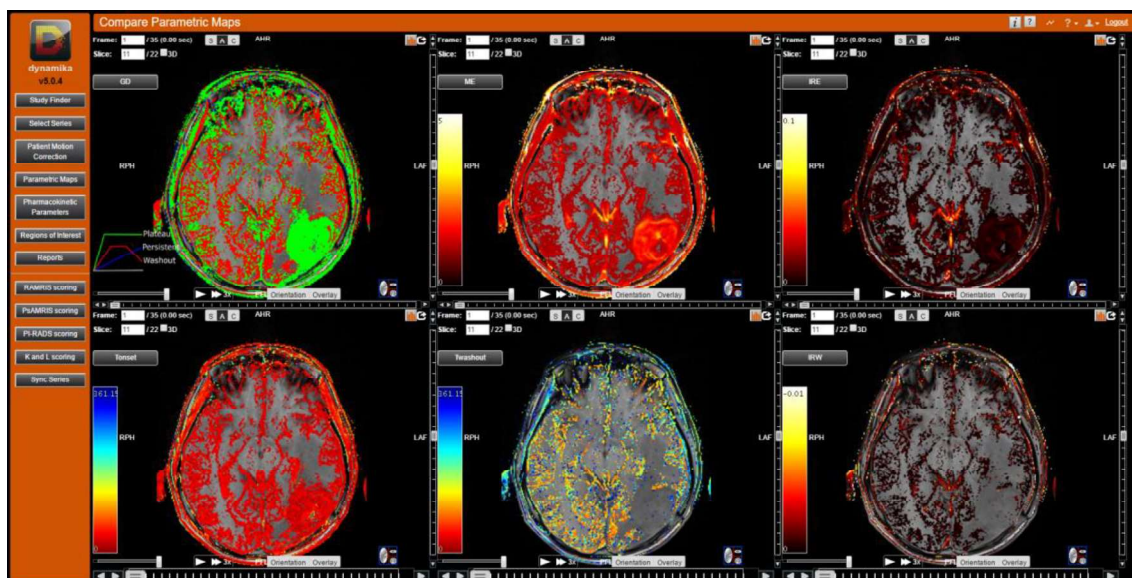
The Compare Parametric Maps screen can be accessed by pressing the "Compare Parametric Maps" button ( ). The Compare Parametric Maps screen can be accessed from any image portlet and is opened in a new tab in the browser. Here you can compare a total of 6 Parametric Maps (cf., Section 4) overlaid on top of the corresponding DCE MRI volume simultaneously. The image portlets are synchronised by time frame and image slice, so that scrolling through frame or slice in one image portlet will update the image accordingly for all portlets.

3.   Patient motion correction

Dynamika offers a fast, robust rigid patient motion correction algorithm to reduce the impact of patient movement during a dynamic image acquisition on subsequent quantitative (pixel-wise) analysis.

Applying the motion correction to a dynamic series is very simple. Select the dynamic scan in the *Select Series* view and then click on *Patient Motion Correction*. The screen will show the non-motion corrected series in the left hand portlet. Press the "Run" button and the motion correction algorithm will start to create the motion corrected series. If desired, you can select a time frame as the reference image, to which other images in the series will be aligned. It is recommended that you use the first time frame or the time frame which occurs just before the contrast agent is introduced into the subject's bloodstream as the reference image.

Once the motion corrected series has been calculated, it will appear in the right hand image portlet. The motion correction algorithm will normally take between 10 seconds and 1 minute to complete for normal clinical datasets, for series with a very high resolution or a high number of timeframes, it may take longer.

The motion corrected series will automatically be created as a new series in the study, and can be found in the *Select Series* view. It is clearly marked as motion corrected in the "Series Description" DICOM tag to avoid confusion between processed and unprocessed images. It is recommended to work with the motion corrected series in subsequent analysis.

⚠️**CAUTION**

Rigid motion correction is designed to reduce gross patient motion, but does not compensate for internal or other non-rigid deformations. Please always evaluate the complete motion corrected dynamic series before continuing to work with any motion corrected data.

4.   Parametric Maps

Parametric maps are a method of quantifying and classifying pixel-wise signal-time curve morphology in a DCE-MRI scan. For DCE-MRI acquisition guidelines, please refer to Appendix B.

Dynamika's parametric maps offer pixel-wise analysis of signal-time curve morphology and heuristic parameters such as maximum enhancement (ME), initial rate of enhancement (IRE) and others to give insight into physiological factors of inflammatory response, blood-brain barrier integrity, or endothelial permeability in the underlying tissue. Calculation and pixel-wise analysis of parametric maps are handled in the *Parametric Maps* view.
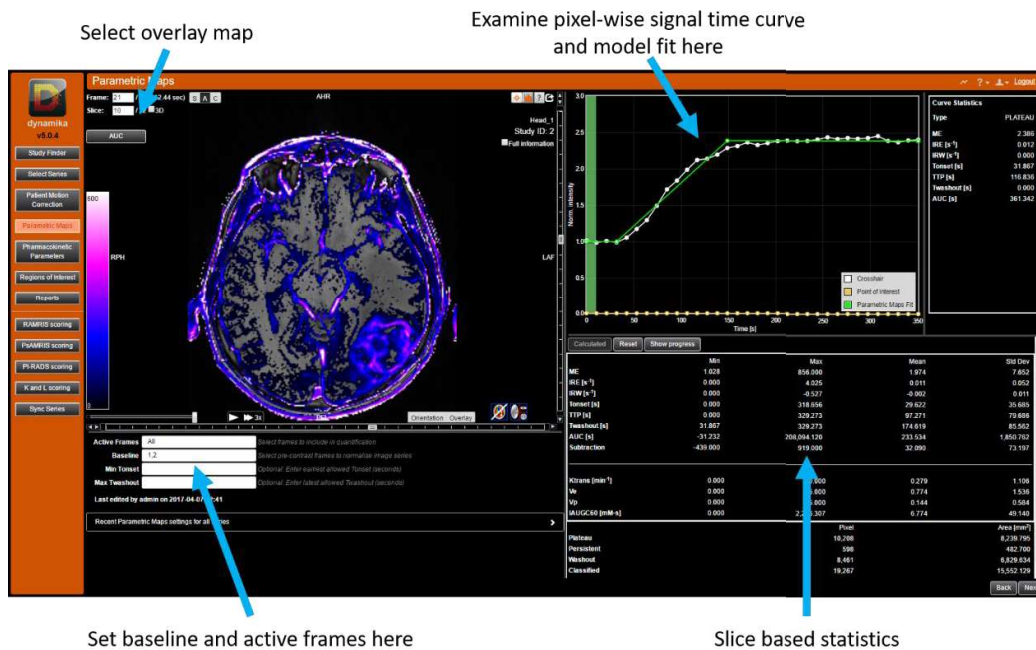
The Baseline Frames should be set as the number of frames, e.g. frame 1-4, which occur *before* contrast agent injection. For reliable analysis, the system requires a minimum of two baseline frames. Using both knowledge of the acquisition protocol and by examining the signal-time curve in the upper right hand pane which contains the graph, set the baseline frames in the appropriate field. The green column in the signal-time graph shows visually which frames are used as baseline.

> **i** If there appears to be an increase in signal within the green highlighted region of the graph, you may need to consider adjusting the baseline frames. It is advisable to examine signal time curves from multiple regions of the image to set baseline frames accurately.

The number of considered frames can be limited by changing the Active Frames. This can be useful for limiting very long scans or when considering data with large variations in post contrast dynamic coverage.

⚠️**CAUTION**

Please evaluate the quality of resulting parametric maps in regions of interest to ensure that image artefacts such as motion or high image noise does not affect the fitting quality before extracting quantification results and statistics from said region.

> **i** The quality of the parametric maps algorithm output can be reviewed by visually examining the appearance of the calculated maps as well as by visually examining the quality of fit for selected voxels by hovering with the mouse cursor over the region of interest and comparing the Parametric Maps Fit to the original normalized intensities in the displayed graph.
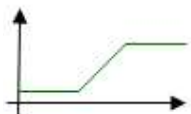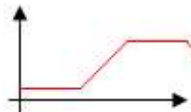
4.1   Parametric Map Definitions and Algorithm

The analysis of the data starts by normalising each signal intensity vs. time curve to the average baseline signal intensity.

Behaviour of the signal intensity vs. time curves may be explained by the underlying phases of the data acquisition. Starting from a baseline, the perfused tissues absorb the contrast agent, and their intensity climbs up (wash-in phase); it usually increases up to a certain point and then exhibits a plateau (of variable width) followed by a wash-out phase (gradual signal intensity decrease).
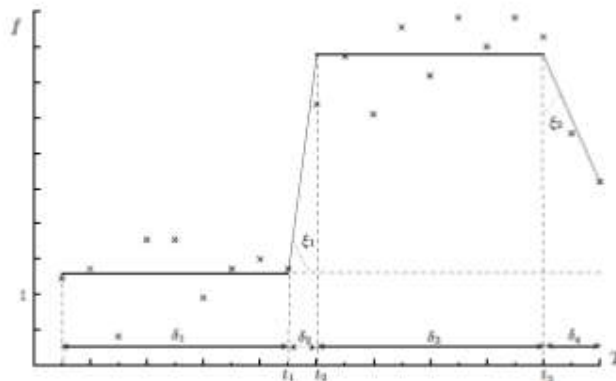
The shape of each (normalized) pixel signal time curve is classified using one of four models and the classification result is visualized in the GD map

	Model: M0 Negligible enhancement. Some tissues within cortical and trabecular bone, inactive joints, skin and disease unaffected areas do not absorb Gd-DTPA and are not expected to show intensity enhancement in the later frames of temporal slices. In practice, any voxel for which the maximum enhancement does not exceed the estimated noise level of the volume by a fixed multiplier (under consideration of the local neighbourhood) are automatically classified as non-enhancing and hence excluded from further parametric analysis. Colour in GD uptake maps – no colour
	Model: M1 Persistent Enhancement. *Base/wash-in*. There is often a proportion of curves in which by the end of the scanning procedure the maximal intensity has not been reached, indicating constant leakage into locally available extra-cellular space. The Gd-DPTA absorption and signal intensity vs. time curves enhancing continues after the scanning has been completed. Colour in GD uptake maps – blue
	Model: M2 Plateau Enhancement. *Base/wash-in/plateau*. Full absorption of the Gd-DTPA by the tissues. Starting from the baseline, it is possible to observe distinguished wash-in and plateau pattern of enhancement. Colour in GD uptake maps – green
	Model: M3 Wash-out Enhancement. *Base/wash-in/plateau/wash-out*. The wash-out phase is observed at the end of the scanning procedure. Colour in GD uptake maps – red

For each model the piecewise linear best fit is determined in a least-squares sense, and the model with the smallest fitting error is automatically selected. Other than the definition of the baseline frames and the number of considered frames during analysis (active frames), which allows the user to limit the post contrast duration of the dynamic acquisition that is considered during the analysis (see above), this algorithm is fully automatic and does not allow the user to set any further inputs to influence the classification results. From these model fits, a number of parameters are extracted:
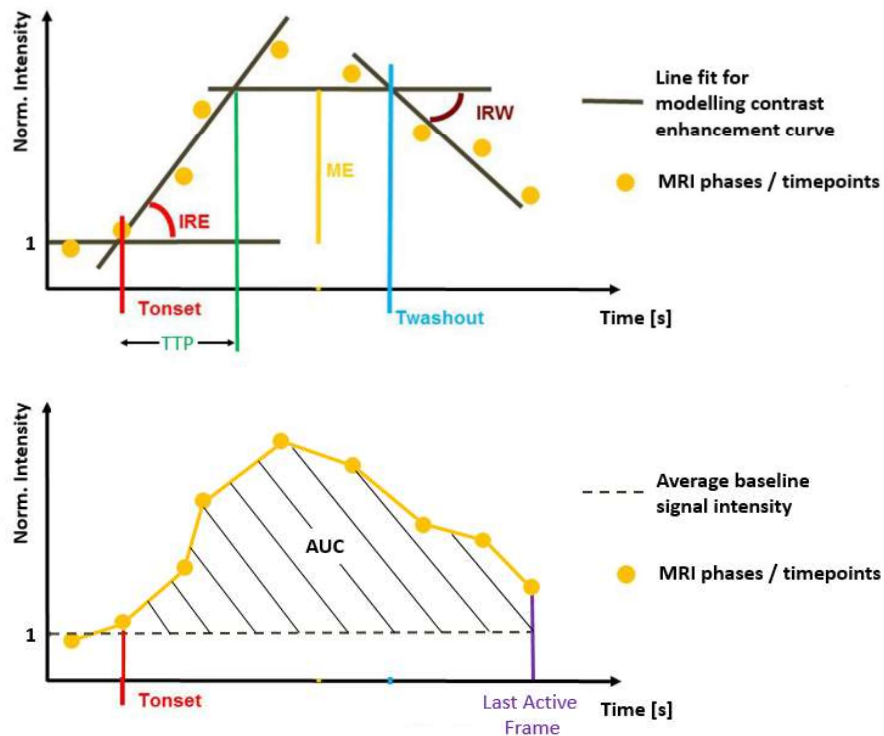
Quantity	Symbol	Units	Description
Maximum enhancement	ME	unitless	Ratio between plateau and baseline intensity
Initial rate of enhancement	IRE	s^{-1}	Slope of the enhancement (wash-in) phase
Initial rate of washout	IRW	s^{-1}	Slope of the washout phase
Time of onset	Tonset	s	Time difference between start of scan and start of enhancement
Time to peak	TTP	s	Time difference between the start of the enhancement and the plateau phase
Time to washout	Twashout	s	Time difference between start of scan and the end of the plateau phase / start of wash-out phase
Area und the curve	AUC	s	Area between baseline intensity and the normalized intensity curve

> **i** Voxels with no or only negligible enhancement (Model: M0), which are not coloured in the Parametric Map, are not considered when computing slice-based or ROI-based statistics on said parameter.

From these parameters, in combination with the volume of the enhancing voxels, the following DEMRIQ parameters[1] can be directly derived from previously detailed parametric maps for any delineated region of interest (see also Section 6):

Quantity	Units	Description
DEMRIQ-Vol	ml	Volume of all voxels classified as either Plateau or Washout (model M2 or M3) within a ROI
DEMRIQ-ME	ml	Product of DEMRIQ volume and mean ME within a ROI
DEMRIQ-IRE	ml/s	Product of DEMRIQ volume and mean IRE within a ROI

i	DEMRIQ parameters are not displayed by the software directly.
	To access DEMRIQ parameters for slice ROIs / volume ROIs, please generate a report including Parametric Maps parameters via the Reports page (see also Section 7).

The following example screenshot highlights the DEMRIQ parameters in an exported .xls report.

After intraveneous Gd injection, Gd passes into the interstitial space at a rate dependent on local capillary permeability and tissue perfusion. The resulting Gd-based T1 shortening is imaged by DCE-MRI as an increase in signal intensity over time. While DEMRIQ-Vol, which in the literature is sometimes also referred to as Nvoxel, corresponds to the volume of enhancing voxels (in ml) with Plateau or Washout patterns within a region of interest, DEMRIQ-IRE and DEMRIQ-ME represent composite variables reflecting both the volume and degree of enhancement and are in the literature sometimes also simply denoted as IRExNvoxel and MExNvoxel, respectively.

i	Aforementioned descriptive parameters are derived from T1-weighted Dynamic Contrast Enhanced (DCE) MRI, which should not be confused with Dynamic Susceptibility Contrast (DSC) MRI for perfusion analysis, which is not supported by Dynamika.

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[1] Kubassova OA, Boesen M, Østergaard M, et al, "DEMRIQ: A Dynamic Contrast Enhanced MRI Quantification Method for Objective Assessment of Treatment Response in Patients with Inflammatory Arthritis" RSNA 2014 Scientific Assembly and Annual Meeting (SSK14-06)

5. Pharmacokinetic Parameters

Dynamika offers pharmacokinetic parameters derived from the widely used Kety-Tofts model of contrast agent retention in tissue. Two implementations of the model are offered the "Standard Tofts" model and the "Extended Tofts" model, which are detailed in Section 5.1. For DCE-MRI acquisition guidelines, please refer to Appendix B.

The calculation and analysis of pharmacokinetic parameters is all handled in the *Pharmacokinetic Parameters* view.

Pharmacokinetic calculation settings

Slice statistics

Pixel-wise Gadolinium concentration curves with fitted parameters
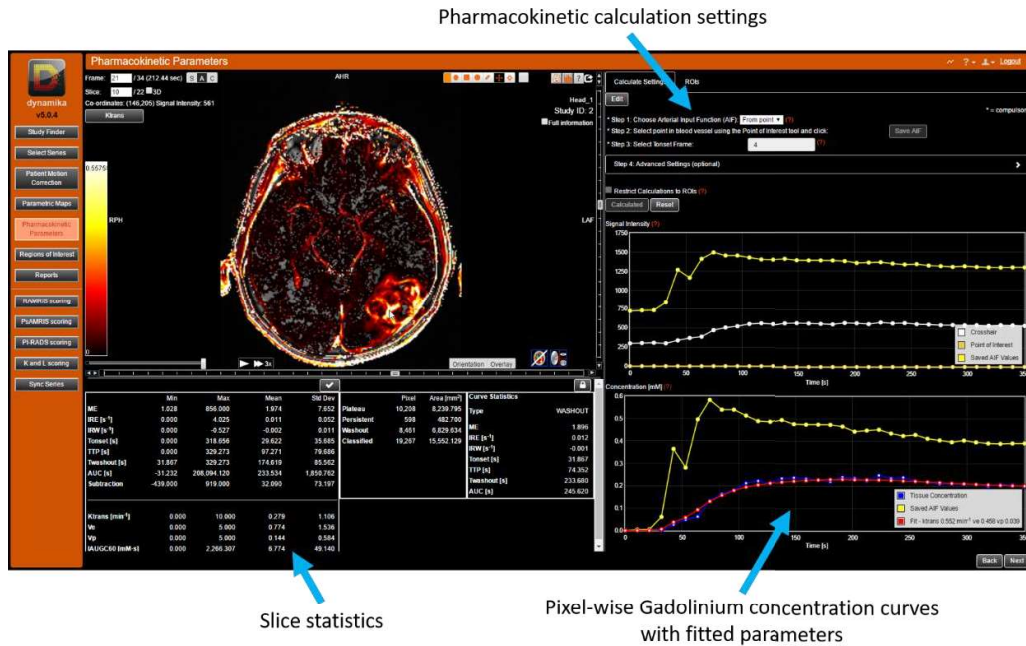
The *Pharmacokinetic Parameters* view provides an image portlet to view the pharmacokinetic parameter maps, slice statistics, access to adjust calculation settings and pixel query graphs to show the arterial input function (AIF) and contrast signal-time/concentration-time curves.

⚠️ **CAUTION**

Please evaluate the quality of resulting pharmacokinetic parameters in regions of interest to ensure that image artefacts such as motion or high image noise do not affect the fitting quality before extracting quantification results and statistics from said region. Evaluation of such quality of fit should be based on judgement and experience of a suitably qualified physician.
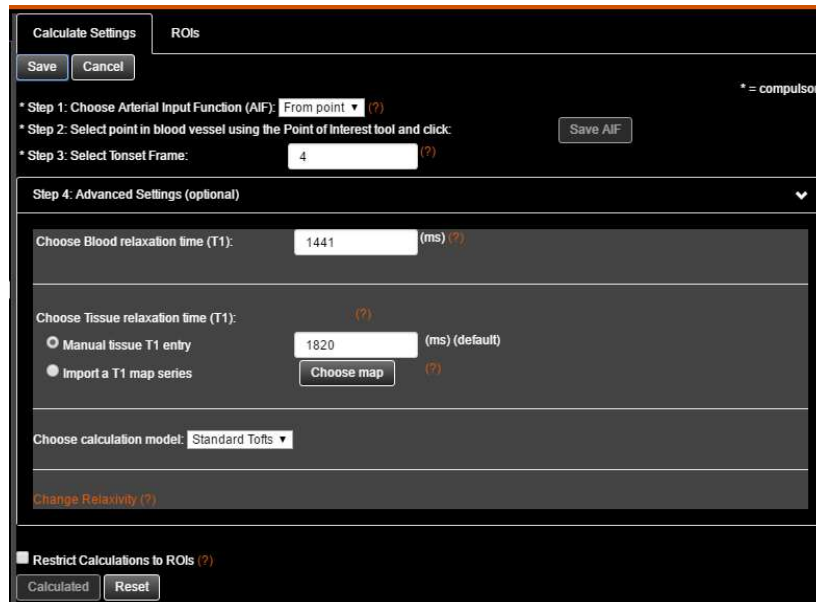
> **i** The quality of the pharmacokinetic parameters algorithm output can be reviewed by visually examining the appearance of the calculated maps as well as by visually examining the quality of fit for selected voxels by hovering with the mouse cursor over the region of interest and comparing the Pharmacokinetic Parameters Fit to the original concentrations in the displayed graph.

5.1 Calculation settings

To conduct a successful pharmacokinetic analysis, the first step is to set the appropriate calculation settings, which can be accessed in the top right area of the *Pharmacokinetic Parameters* view.

To start entering settings, press the "Edit" button at the top of the *Calculate Settings* tab, the parameters are then available for editing. Click also on the *Advanced Settings* bar to unfold the advanced settings menu. All settings must be set appropriately to ensure proper calculation of pharmacokinetic parameters:

The following is a guide to set the parameters properly for successful pharmacokinetic analysis:

- Arterial Input function:
  There are two options to set the AIF:

  - Manual selection "From point": choose a point of interest (POI) in a clearly identifiable and anatomically relevant artery which can be found in the DCE-MRI image. Once you have placed the POI, press "Save AIF" and the AIF will be set. Overlaying a map such as the subtraction map or the IRE map may be helpful to locate an artery.
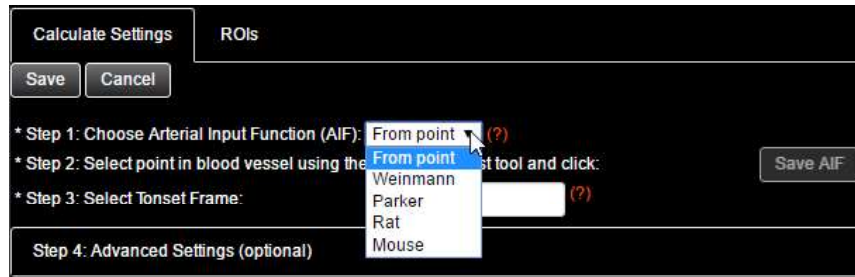
- Predefined population model AIF: Dynamika provides 4 separate population models including 2 pre-clinical models for rats and mice. This may be helpful if an artery is not clearly identifiable in the DCE-MRI image:

  - Weinmann model[9]: The Weinmann model is based on a bi-exponential model and requires the user to specify the injected contrast agent dose (default: 0.1 mmol/kg) and the time frame corresponding to the *peak* of the bolus at the region of interest (Peak Frame).

  - Parker model[10]: The Parker model can be described as a mixture of two Gaussian functions and an exponential modulated by a sigmoid. Like the Weinmann model, the user is required to specify the injected contrast agent dose (default: 0.1 mmol/kg) and the time frame corresponding to the *onset* of the bolus at the region of interest (Tonset Frame).

  - Rat model[11] / Mouse model[12]: Both pre-clinical models are based on bi-exponential functions similarly to the Weinmann model, but with a linear upslope between Tonset and Tpeak. The user is required to specify the injected contrast agent dose (in mmol/kg) and the time frames corresponding to the *onset* and *peak* of the bolus at the region of interest (Tonset and Peak Frame).

- Tonset Frame: This is the time-frame just before contrast enters the anatomical region of interest and is used to compute the initial area under the gadolinium concentration curve (IAUGC60) and potentially to characterize the selected population model AIF. This should be set bearing in mind both the acquisition protocol, and also visual analysis of concentration time curves in the DCE-MRI image.

- Blood relaxation time: This should be set appropriately using a value derived from the literature and/or specific knowledge or measurements for the scan. The blood relaxation time (given in ms) is dependent on the magnetic field strength of the

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[9] Weinmann H.J, *et al.* "Pharmacokinetics of GdDTPA/dimeglumine after intravenous injection into healthy volunteers." Physiol Chem Phys Med NMR 1984; 16: 167–72. Medline, ISI

[10] Parker G.J *et al.* "Experimentally-derived functional form for a population-averaged high-temporal-resolution arterial input function for dynamic contrast-enhancedMRI." Magn Reson Med. 2006 Nov;56(5):993-1000.

[11] McGrath D.M, *et al.* "Comparison of model-based arterial input functions for dynamic contrast-enhanced MRI in tumor bearing rats*."* Magn Reson Med. 2009 May;61(5):1173-84.

[12] Loveless M.E, *et al.* "A quantitative comparison of the influence of individual versus population-derived vascular input functions on dynamic contrast enhanced-MRI in small animals." Magn Reson Med. 2012 Jan;67(1):226-36.

scanner and other factors. In humans, commonly used values are 1441ms for a 1.5T scanner or 1664ms for a 3T scanner.

- Tissue relaxation time: There are two approaches for defining the tissue relaxation time:

  - Manual tissue T1 entry: choose an appropriate value, derived from literature or other prior knowledge of the tissue of interest.

  - T1 can be measured specifically in each voxel before a DCE-MRI scan using a variable flip angle (VFA) acquisition, which should be taken in the same acquisition as the DCE-MRI scan itself. If a VFA series has been uploaded as part of the study and you wish to use it, select "Import a T1 map series", press "Choose map" and a popup appears that will allow you to select the corresponding T1 map derived from the VFA series and to press the "Import" button to return to the previous screen.
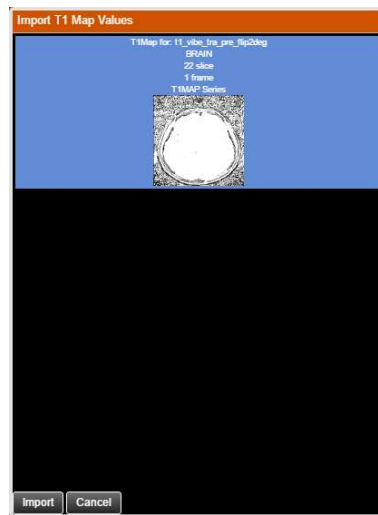
The pre-contrast T1 values at each voxel location are calculated from the signal intensities at each flip-angle using a linear curve fitting method as described by the QIBA DCE MRI Quantification Profile [13]. The slice locations, orientations and resolution of the VFA images should be prescribed identically to the corresponding dynamic series (see also Appendix B1).

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[13] DCE MRI Technical Committee. DCE MRI quantification profile, quantitative imaging biomarkers alliance. QIBA, 2012.

- Pharmacokinetic calculation model:

Dynamika offers two commonly used models[14,15] for pharmacokinetic analysis, the "Standard Tofts" model and the "Extended Tofts" model, each with specific benefits in specific applications. Choose here the preferred model to use for calculation. The "Standard Tofts" model yields parameters Ktrans and Ve, while the "Extended Tofts" model yields both Ktrans and Ve along with a further parameter Vp.

Standard Tofts model equation:

$$C_t(t) = K^{trans} \int_0^t C_p(\tau) e^{\frac{K^{trans}}{v_e}(t-\tau)} d\tau$$

Extended Tofts model equation:

$$C_t(t) = v_p C_p(t) + K^{trans} \int_0^t C_p(\tau) e^{\frac{K^{trans}}{v_e}(t-\tau)} d\tau$$

Given the tissue uptake curve $C_t(t)$ and the AIF, the free parameters of the model (highlighted in orange) are estimated using an established Levenberg-Marquardt fitting algorithm[13], which requires adequate baseline sampling (see Section B3).

i

Voxels with negligible enhancement, i.e., any voxel for which the maximum enhancement does not exceed the estimated noise level of the volume by a fixed multiplier (under consideration of the local neighbourhood) are automatically excluded from pharmacokinetic analysis (see Parametric Model M0 in Section 4.1).

Voxels with no or only negligible enhancement, which are not coloured in the Pharmacokinetic Map, are not considered when computing slice-based or ROI-based statistics on said parameter.

- Contrast agent relaxivity:

Different contrast agents have different relaxivity values and this must be set correctly to ensure accurate pharmacokinetic parameters. For example, the relaxivity of Gd-DTPA (Magnevist) is usually assumed to be equal to the in vitro value of 4.5 $s^{-1}·mM^{-1}$ (measured at 1.5T)[16], which is configured as the default parameter value, although it may be different in vivo.

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[14] P. S. Tofts et al., "Estimating kinetic parameters from dynamic contrast-enhanced T 1- weighted MRI of a diffusable tracer: standardized quantities and symbols," Journal of Magnetic Resonance Imaging, vol. 10, no. 3, pp. 223–232, 1999.

[15] P. S. Tofts, "Modeling tracer kinetics in dynamic Gd-DTPA MR imaging," Journal of Magnetic Resonance Imaging, vol. 7, no. 1, pp. 91-101, Jan. 1997.

[16] Tofts, P.S. and Parker, G.J.M. (2013) "DCE-MRI: acquisition and analysis techniques", in Barker, P.B., Golay, X., and Zaharchuk, G. (eds.) Clinical Perfusion MRI: Techniques and Applications. Cambridge: Cambridge University Press, pp. 58–74.

Relaxivity depends on the temperature, field strength, and substance in which the contrast agent is dissolved. For contrast agents in clinical use, it is typical to cite relaxivity values at 1.5T in plasma at body temperature (37°C).

To change the T1 (longitudinal) relaxivity, click "Change Relaxivity". This opens a new popup, which includes for the user's convenience relaxivities in plasma and in water at different magnetic field strengths based on the publication of Rohrer et al.[17], which shows good agreement between data measured in plasma and in whole blood, assuming similar relaxivities in human blood (within the given error ranges).

In conclusion, Rohrer et al. suggest the use of values obtained in plasma at the field strengths of interest (currently, mainly 1.5T and 3.0T) while avoiding relaxivity values determined in water and/or at 0.47T unless required by specific investigations.

Change Relaxivity

Enter relaxivity value (default 4.5 $s^{-1} \cdot mM^{-1}$): 4.5

[Change] [Cancel]

Typical values of longitudinal relaxivity for a range of commercially available contrast media
Warning: Not all compounds might be approved for clinical use in all countries.

Relaxivities [$s^{-1} \cdot mM^{-1}$] in Plasma

Contrast Brand Name	0.47 Tesla	1.5 Tesla	3.0 Tesla	4.7 Tesla
MAGNEVIST	3.8 +/- 0.2	4.1 +/- 0.2	3.7 +/- 0.2	3.8 +/- 0.2
GADOVIST/GADAVIST	6.1 +/- 0.3	5.2 +/- 0.3	5.0 +/- 0.3	4.7 +/- 0.2
PROHANCE	4.8 +/- 0.2	4.1 +/- 0.2	3.7 +/- 0.2	3.7 +/- 0.2
MULTIHANCE	9.2 +/- 0.5	6.3 +/- 0.3	5.5 +/- 0.3	5.2 +/-0.3
DOTAREM	4.3 +/- 0.2	3.6 +/- 0.2	3.5 +/- 0.2	3.3 +/- 0.2
OMNISCAN	4.4 +/- 0.2	4.3 +/- 0.3	4.0 +/- 0.2	3.9 +/- 0.2
OPTIMARK	5.7 +/- 0.3	4.7 +/- 0.3	4.5 +/- 0.3	4.4 +/- 0.2
ABLAVAR/MS-325	28 +/- 1	19 +/- 1	9.9 +/- 0.5	6.9 +/- 0.3
PRIMOVIST/EOVIST	8.7 +/- 0.4	6.9 +/- 0.4	6.2 +/- 0.3	5.9 +/- 0.3

Relaxivities [$s^{-1} \cdot mM^{-1}$] in Water

Contrast Brand Name	0.47 Tesla	1.5 Tesla	3.0 Tesla	4.7 Tesla
MAGNEVIST	3.4 +/- 0.2	3.3 +/- 0.2	3.1 +/- 0.3	3.2 +/- 0.2
GADOVIST/GADAVIST	3.7 +/- 0.2	3.3 +/- 0.2	3.2 +/- 0.3	3.2 +/- 0.2
PROHANCE	3.1 +/- 0.2	2.9 +/- 0.2	2.8 +/- 0.2	2.8 +/- 0.1
MULTIHANCE	4.2 +/- 0.2	4.0 +/- 0.2	4.0 +/- 0.3	4.0 +/- 0.2
DOTAREM	3.4 +/- 0.2	2.9 +/- 0.2	2.8 +/- 0.2	2.8 +/- 0.1
OMNISCAN	3.5 +/- 0.2	3.3 +/- 0.2	3.2 +/- 0.3	3.3 +/- 0.2
OPTIMARK	4.2 +/- 0.2	3.8 +/- 0.2	3.6 +/- 0.3	3.8 +/- 0.2
ABLAVAR/MS-325	5.8 +/- 0.3	5.2 +/- 0.3	5.3 +/- 0.3	5.5 +/- 0.3
PRIMOVIST/EOVIST	5.3 +/- 0.3	4.7 +/- 0.2	4.3 +/- 0.3	4.9 +/- 0.2

Rohrer et al., "Comparison of magnetic properties of MRI constrast media solutions at different magnetic field strengths", vol. 40, no.11, pp. 715-724 Investigative Radiology, Nov. 2005

Change the value in the field to reflect the contrast agent used and magnetic field strength then press "Change" in order to set the value.

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[17] Rohrer M, Bauer H, Mintorovitch J, et al. "Comparison of magnetic properties of MRI contrast media solutions a different magnetic field strengths." Invest Radiol 2005; 40:715-724.

Once the above steps have all been completed successfully, pharmacokinetic parameters can be calculated. Press the "Save" button at the top of the *Calculate Settings* tab if you are ready, and then press "Calculate".

Calculation of pharmacokinetic parameters for the whole volume in normal clinical datasets should normally take between 30 seconds and 2-3 minutes, depending on the dimensions of the series and the number of timeframes.

To save time in calculation, you may want to utilise the "Restrict Calculations to ROIs" option. To use this option, create regions of interest surrounding the specific tissue of interest (please see Section 3 Patient motion correction in this manual for information on managing ROIs), then select the "Restrict Calculations to ROIs" checkbox. Please note: the "Restrict Calculations to ROIs" option can only be invoked in the "Edit" mode of the *Calculate Settings* tab. If you cannot choose the option, press the "Edit" button at the top of the *Calculate Settings* tab and choose it, then press "Save" and press "Calculate".

i	If the calculation of pharmacokinetic parameters has been restricted to ROIs, resulting maps will not be defined in other areas of the volume and hence pharmacokinetic information will not be available for any newly drawn or modified ROIs.

| Quantity	Symbol	Units	Type
Flip angle	FA	degrees	Fixed (from DICOM)
Haematocrit	Hct	%	Fixed (42%)
T_1 relaxivity	r_1	$s^{-1} \cdot mM^{-1}$	Free (input) Default: 4.5 $s^{-1} \cdot mM^{-1}$
T_1 of blood	T_{10}(blood)	ms	Free (input) Default: 1400ms
T_1 of tissue	T_{10}(tissue)	ms	Free (input) or via imported T_1 map
Injected contrast agent dose	D	mmol/kg	Free (input) Default: 0.1 mmol/kg
Onset frame	Tonset	unitless (frame index)	Free (input)
Peak frame		unitless (frame index)	Free (input) *Only for certain AIFs*
Transfer constant	Ktrans	min^{-1}	Free (output)
Fractional volume of EES	Ve	Typically $0 < Ve < 1.0$	Free (output)
Fractional volume of plasma in tissue	Vp	Typically $0 < Vp < 1.0$	Free (output)
Initial area under Gd concentration curve for 60s	IAUGC60	mM·s	Free (output)

i

Ve and Vp, when interpreted as volume fractions, are expected to range between 0% and 100%. However, the Tofts model itself does not restrict any of the free parameters to specific value ranges such that fitted parameters outside of this range can be observed under certain circumstances (after successful Least Squares Fitting). In fact, the accuracy of any fitted parameter is limited by how accurately the input parameters can be determined. Ve and Vp values above 1.0 are often caused by incomplete data or if T_{10} is wrong for specific voxels[18] without negatively affecting the goodness of fit.

While Dynamika does not constrain the output parameters to the typically expected range, the output parameters are automatically limited (cropped) to: $0 \leq Ve \leq 5.0$, $0 \leq Vp \leq 5.0$, and $0 \leq kTrans \leq 10.0$. This is done to avoid values extremely outside the expected range, which could over proportionally affect any ROI statistics (such as the mean value) and negatively affect the performance of the analysis.

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[18] P. S. Tofts et al., "Quantitative Analysis of Dynamic Gd-DTPA Enhancement in Breast Tumors Using a Permeability Model," Magnetic Resonance in Medicine, vol. 33, no. 4, pp. 564–568, 1995.
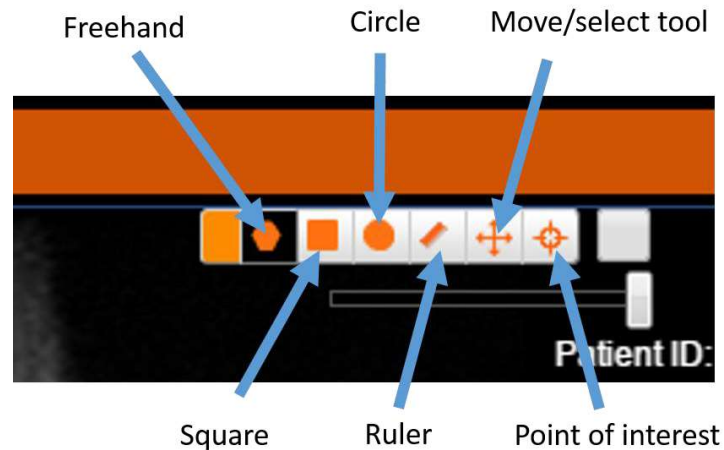
6. Regions of Interest

The *Regions of Interest* view offers multiple tools to outline regions of interest (ROIs) in medical images and then derive statistics from those ROIs.
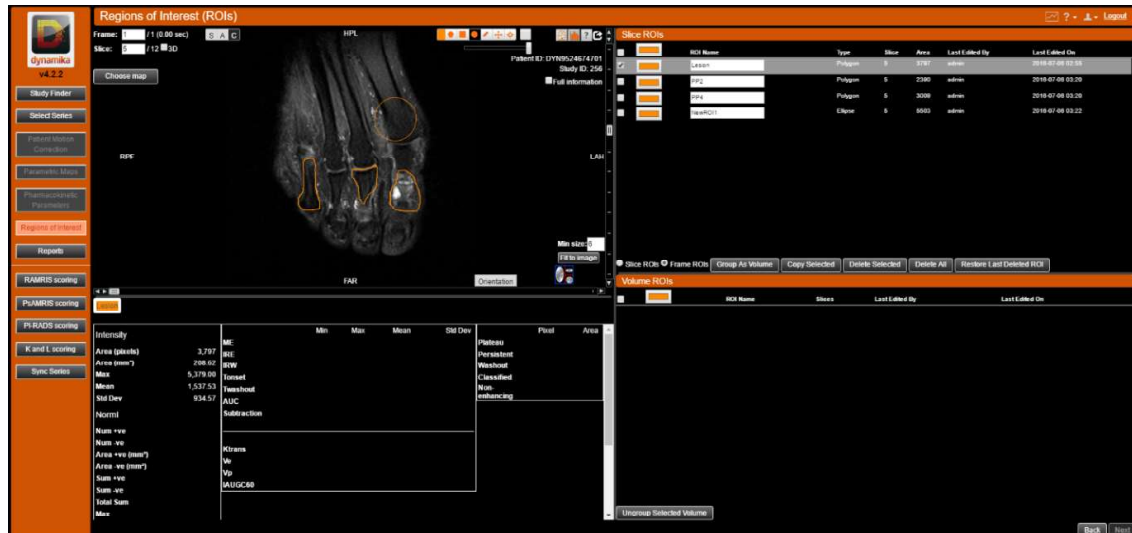
A ROI is defined in Dynamika as a boundary which surrounds a particular feature of interest, any pixel (or voxel) which is in the interior the boundary of the ROI will be considered as belonging to that ROI, and therefore any quantities associated with that pixel, such as signal intensity or a quantitative map parameter such as Ktrans, will be included in statistics drawn from that ROI, such as the average value, maximum value or standard deviation.


Dynamika offers 3 different ROI definition tools, a freehand ROI tool, a square ROI tool and a circular ROI tool, which can be seen in the tool palette below:

Freehand   Circle   Move/select tool

Square   Ruler   Point of interest

Other tools available in the *Regions of Interest* view, and also in other views which have ROI functionality (such as the *Pharmacokinetic Parameters* view), include the (RECIST) ruler, the move/select ROI tool, and the Point of Interest (POI) tool.

To draw a ROI, select the desired tool in the tool palette and click with the left mouse button in the image, then drag the mouse until the ROI is of the desired shape and size. For the freehand tool, click and drag the mouse pointer along the path you wish to draw the contour, then when you release the mouse button, the ROI will automatically join to create a closed contour.

The move/select tool can be used to move, resize and select ROIs for deletion. To select a ROI, enable the move/select tool and click in the region near the ROI, this will select it, if you now move the cursor while holding down the select tool, the ROI will move. By double clicking a ROI, you can reveal the bounding box. You can resize the ROI by clicking and dragging one of the square handles.
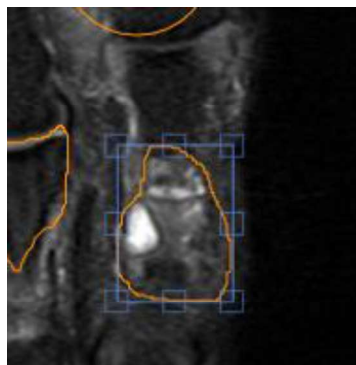
Regions of interest can be managed in the pane on the right hand side of the *Regions of Interest* view:
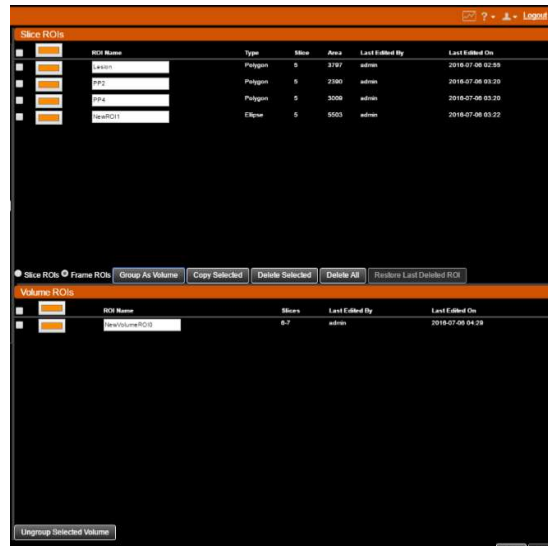
Here you can select ROIs, delete them, rename and colour them. The checkboxes on the left hand side select ROIs to be acted upon. The statistics of all ROIs selected here will be detailed in tabs in the bottom left hand side of the *Regions of Interest* view.

Two types of ROIs are available in Dynamika, *Volume ROIs* and *Slice ROIs.* Volume ROIs (also referred to as VOIs) are a collection of slice ROIs in contiguous slices joined together to form a volumetric object. They can be used to define a tissue feature or organ in 3 dimensions. To create a volume ROI, outline the object of interest in all slices in which it is visible with slice ROIs. Then, select all the ROIs you have just created and click "Group As Volume". The new volume ROI will now appear in the Volume ROIs pane. The volume ROI can also be reverted back to the individual slice ROIs by clicking "Ungroup Selected Volume".

i	The software does not constrain the user in combining an arbitrary selection of ROIs into one VOI and the user should take caution that the volume of interest has been carefully delineated on all slices without missing intermediate slices.

To delete a ROI, select the checkbox to the left hand side of the undesired ROI, then press the button labelled "Delete Selected". The most recently deleted ROI can be restored, by pressing "Restore Last Deleted ROI".

6.1   Fit ROI to image

In the presence of a Parametric Map (see Section 4), the outline of a (slice) ROI can be automatically adjusted based on the visualized Parametric Map to only outline coloured voxels (unequal to zero). When selecting a ROI and pressing the Fit to Image button in the image portlet (bottom right corner), Dynamika will automatically grow and shrink the contour such that all coloured voxels within the original ROI and all connected coloured voxels (within the current plane) will be included in the newly created ROI with all non-coloured voxels being outside the ROI. In practice, this operation is equivalent to a 2D Region

Growing operation where voxels with a Parametric Map value unequal to zero are included if connected to the seed-points (here coloured voxels within the original ROI).
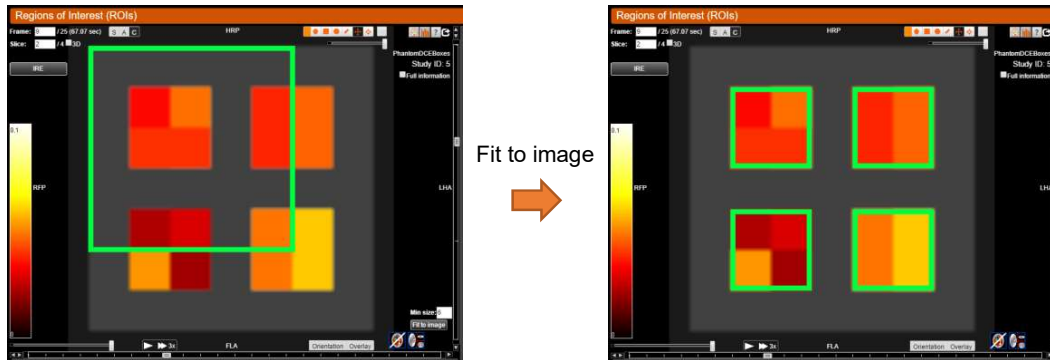
Fit to image

After the Fit to Image operation, Dynamika will show the original as well as the fitted contour and ask the user to confirm the result. If pressing the OK button (also bottom right corner of image portlet), the original ROI will be deleted and the fitted ROI is considered approved. Alternatively, if pressing the Cancel button, the fitted ROI will be discarded.

> **i**
>
> The Fit to Image functionality is only available for DCE-MRI with a calculated and displayed Parametric Map. Only one 2D ROI can be fitted to the content of the displayed Parametric Map at a time.

7.   Reporting and scoring

For clinical observational studies, Dynamika offers interactive integrated scoring systems for different applications in oncology and rheumatology such as RAMRIS, PsAMRIS, PIRADS and K and L scoring. Readers can simultaneously view radiological images and complete the scoring forms in Dynamika with a unified workflow. The various reports can be accessed using the tabs in the lower portion of the left-hand sidebar:

- **OMERACT Rheumatoid Arthritis MRI scoring system (RAMRIS)**

Once you have selected the series to assess, press the RAMRIS scoring button, and the form will open in a new tab. This allows you to visualise your MRIs and at the same time complete the score form for metacarpophalangeal (MCP) and wrist joints. The form is based on the publication of Østergaard et al.[19] and subdivided into three parts, Synovitis, Bone erosion, and Bone oedema. The column ID corresponds to the Study ID shown in the corresponding image portlet. In case multiple studies have been selected for longitudinal scoring, additional rows are automatically added to the tables in the form.

There is a dropdown menu, so the score number can be selected for each joint. The work is saved automatically and changes can be made after log in/log out. Though, once you press ''Done'' a warning pop up appears: **''Please note that once you click OK you won't be able to edit your values''.** If you click OK, this automatically lock your study and changes can no longer be made**.** The report is then automatically generated within Dynamika and the results stored securely in the database.

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[19] Østergaard M, Edmonds J, McQueen F, et al "An introduction to the EULAR–OMERACT rheumatoid arthritis MRI reference image atlas" Ann Rheum Dis 2005; 64(Suppl I), pp. i3-i7.

RAMRIS form

Synovitis ▾

OMERACT RAMRIS form for MCP joints

		MCP - joints			
Synovitis (0 - 3)	ID	2	3	4	5
	1	▾	▾	▾	▾

OMERACT RAMRIS form for wrist joints

	ID	Distal radio-ulnar joint	Radio-carpal joint	Intercarpal-CMCJ
Synovitis (0 - 3)	1	▾	▾	▾

Done   Fill empty cells with zero

RAMRIS form

Erosion ▾

OMERACT RAMRIS form for MCP joints

			MCP - joints			
Bone erosion (0 - 10)	ID		2	3	4	5
	1	Proximal	▾	▾	▾	▾
		Distal	▾	▾	▾	▾

OMERACT RAMRIS form for wrist joints

		Base of metacarpal				
Bone erosion (0 - 10)	ID	1	2	3	4	5
	1	▾	▾	▾	▾	▾

	ID	Trapezium	Trapezoid	Capitate	Hamate
Bone erosion (0 - 10)	1	▾	▾	▾	▾

	ID	Scaphoid	Lunate	Triquetrum	Pisiform
Bone erosion (0 - 10)	1	▾	▾	▾	▾

	ID	Distal radius	Distal ulna
Bone erosion (0 - 10)	1	▾	▾

Done   Fill empty cells with zero

RAMRIS form

Oedema ▾

OMERACT RAMRIS form for MCP joints

			MCP - joints			
Bone oedema (0 - 3)	ID		2	3	4	5
	1	Proximal	▾	▾	▾	▾
		Distal	▾	▾	▾	▾

OMERACT RAMRIS form for wrist joints

		Base of metacarpal				
Bone oedema (0 - 3)	ID	1	2	3	4	5
	1	▾	▾	▾	▾	▾

	ID	Trapezium	Trapezoid	Capitate	Hamate
Bone oedema (0 - 3)	1	▾	▾	▾	▾

	ID	Scaphoid	Lunate	Triquetrum	Pisiform
Bone oedema (0 - 3)	1	▾	▾	▾	▾

	ID	Distal radius	Distal ulna
Bone oedema (0 - 3)	1	▾	▾

Done   Fill empty cells with zero

- **OMERACT Psoriatic Arthritis MRI scoring system (PsAMRIS)**

For assessment of peripheral joints in Psoriatic Arthritis, the PsAMRIs scoring form is also integrated to Dynamika. You can visualise your MRIs and at the same time complete your scores for metacarpophalangeal (MCP), proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints. The form is based on the publication of Østergaard et al[20].

Similar to the RAMRIS interactive form, there is a dropdown menu for selecting your score and warning notification before you lock your study.

PsAMRIS form

StudyID: 1   PatientID: 24007

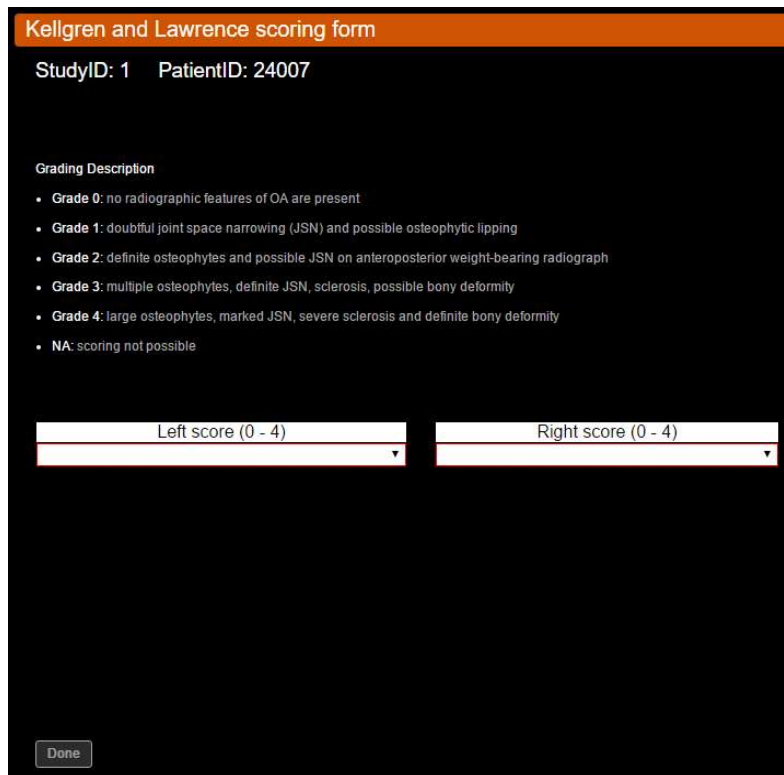|		2. finger	3. finger	4. finger	5. finger
MCP JOINT REGION					
Synovitis *(score 0-3)*		▾	▾	▾	▾
Flexor tenosynovitis *(score 0-3)*		▾	▾	▾	▾
Periarticular inflammation *(score 0 or 1)*	Volar	▾	▾	▾	▾
	Dorsal	▾	▾	▾	▾
Bone oedema *(score 0-3)*	Proximal (M1)	▾	▾	▾	▾
	Distal (M2)	▾	▾	▾	▾
Bone erosion *(score 0-10)*	Proximal (M1)	▾	▾	▾	▾
	Distal (M2)	▾	▾	▾	▾
Bone proliferation *(score 0 or 1)*		▾	▾	▾	▾
PIP JOINT REGION					
Synovitis *(score 0-3)*		▾	▾	▾	▾
Flexor tenosynovitis *(score 0-3)*		▾	▾	▾	▾
Periarticular inflammation *(score 0 or 1)*	Palmar	▾	▾	▾	▾
	Dorsal	▾	▾	▾	▾
Bone oedema score *(score 0-3)*	Proximal (P1)	▾	▾	▾	▾
	Distal (P2)	▾	▾	▾	▾
Bone erosion *(score 0-10)*	Proximal (P1)	▾	▾	▾	▾
	Distal (P2)	▾	▾	▾	▾
Bone proliferation *(score 0 or 1)*		▾	▾	▾	▾
DIP JOINT REGION					
Synovitis *(score 0-3)*		▾	▾	▾	▾
Flexor tenosynovitis *(score 0-3)*		▾	▾	▾	▾
Periarticular inflammation *(score 0 or 1)*	Palmar	▾	▾	▾	▾
	Dorsal	▾	▾	▾	▾
Bone oedema score *(score 0-3)*	Proximal (D1)	▾	▾	▾	▾
	Distal (D2)	▾	▾	▾	▾
Bone erosion *(score 0-10)*	Proximal (D1)	▾	▾	▾	▾
	Distal (D2)	▾	▾	▾	▾
Bone proliferation *(score 0 or 1)*		▾	▾	▾	▾

Done

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[20] Østergaard M, McQueen F, Wiell C, et al "The OMERACT Psoriatic Arthritis Magnetic Resonance Imaging Scoring System (PsAMRIS): Definitions of Key Pathologies, Suggested MRI Sequences, and Prelinary Scoring System for PsA Hands" Journal of Rheumatology 2009; 36:8, pp.1816-1824.

▪ **Kellgren and Lawrence grade (K and L scoring)**

Dynamika also offers a K and L scoring form for classifying the progression of knee osteoarthritis (OA) in plain radiographs (X-rays). The layout of the form is made so that you can assess the target knee (either Right or Left) or both of the knees, according to the needs of a study. This classification was proposed by Kellgren et al. in 1957[21].

Select K and L scoring on the left column and the form will be opened in a new window. Once you complete your scores and press ''done'' the warning pop up will also appear. Once you click ''OK'' the study is locked and the report is automatically generated.

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[21] Kellgren JH, Lawrence JS "Radiological assessment of osteo-arthrosis" Ann Rheum Dis 2000

- **PI-RADS scoring**

Based on the BI-RADS classification for breast imaging, a guideline for MRI of the prostate has been published by the European Society of Urogenital Radiology (ESUR)[22]. The resulting structured reporting scheme (PI-RADS) is available as integrated scoring form including an interactive representation of the 27 Regions of Interest based on the publication of Dickinson et al[23]. When clicking on any of the outlined region, another row is automatically added to the individual scoring table to be completed by the user. Each cell is either a free-form input field or a score number can be selected from a dropdown menu. As before, the report is completed and any inputs are locked upon pressing the "done" button.
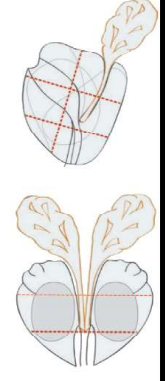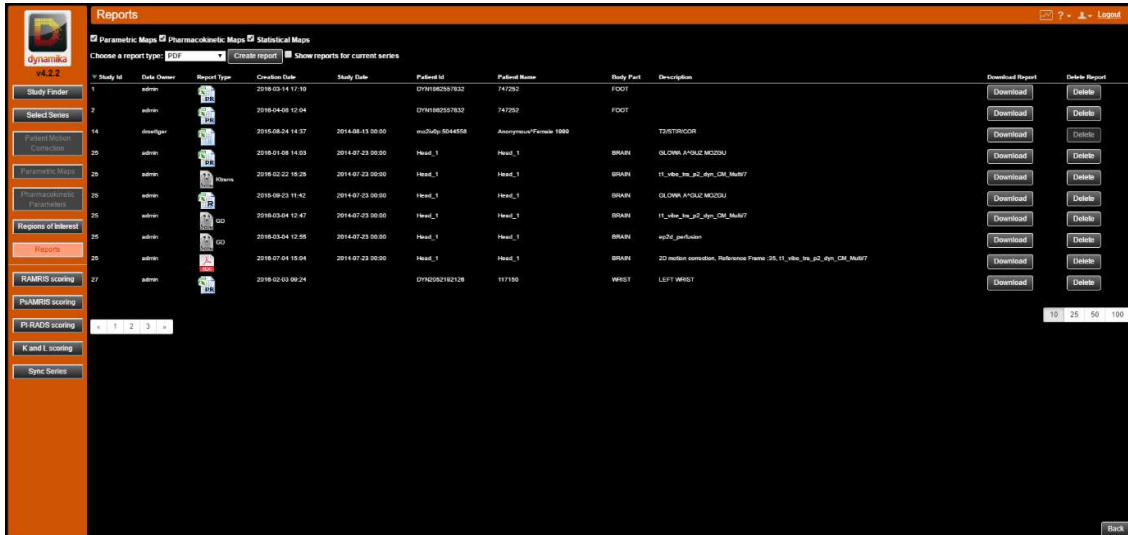

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[22] Barentsz JO, Richenberg J, Clements R, et al "ESUR prostate MR guidelines 2012" Eur Radiol 2012; 22: pp. 746-757.

[23] Dickinson L, Ahmed HU, Allen C, et al "Magnetic Resonance Imaging for the Detection, Localisation, and Characterisation of Prostate Cancer: Recommendations from a European Consensus Meeting" European Urology 2011; 59: pp. 477-494.

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- **Reports**

The *Reports* view gives you access to all the reports you have created in Dynamika for your study. Reports can be generated in PDF or XLS format, and can be downloaded or deleted in the *Reports* view.


| i	Digital signatures embedded into pdf reports (where applicable) follow the format "YYYY.MM.DD HH:MM:SS [Timezone]". For example: 2017.05.04 14:57:39 BST

Appendix A. Instructions to open Anonymization Map with Microsoft Excel
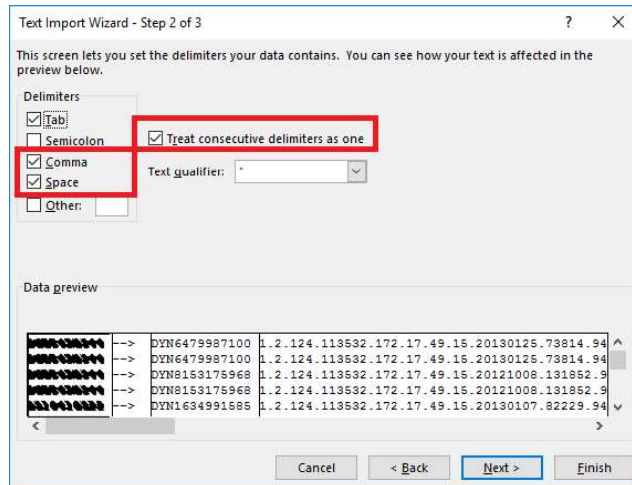
1. Save anonymization map from Dynamika as txt file.

2. Open resulting txt file with Microsoft Excel (or similar)

   - In the Open dialogue select Filter "All Files (*.*)"
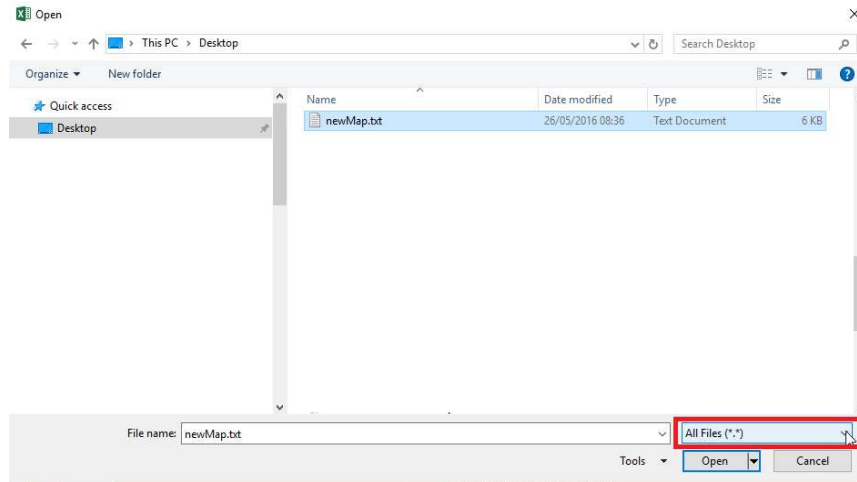
   - In opening Text Import Wizard – Step of 3, select option "Delimited"
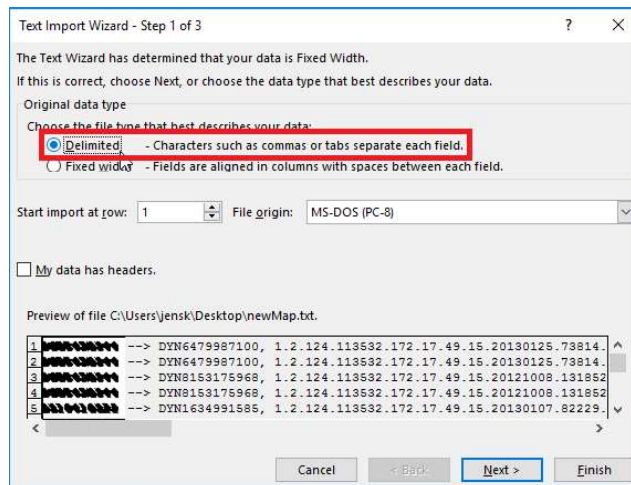
- Text Import Wizard – Step 2 of 3, select Delimeters "Comma" and "Space"; "Treat consecutive delimiters as one".

- Text Import Wizard – Step 3 of 3, format individual columns appropriately, for instance, format the first column as "Text" to avoid that leading zeros are being omitted.
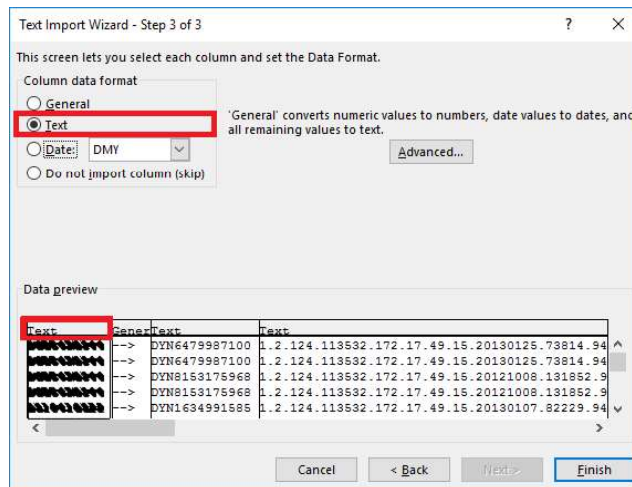
3. The resulting columns equal from left to right
   - A: Patient ID
   - C: Anonymized Patient ID
   - D: Study UID
   - F: Anonymized Study UID
   - G: Series UID
   - I: Anonymized Series UID
   - K: User
   - L: StudyDate

4. Save in xls or xlsx file format

Appendix B. DCE-MRI acquisition guidelines

The following guidelines may be used when acquiring DCE-MRI data for quantitative and semi-quantitative calculations.

B1. Acquisition requirements

To calculate *Parametric Maps* or *Pharmacokinetic Parameters* Dynamika requires a 'dynamic series' which has been acquired from a dynamic contrast-enhanced (DCE) MRI scan. It is recommended that current clinical consensus is followed when acquiring the DCE-MRI scan so that it is compatible with the quantitative and semi-quantitative calculations produced by Dynamika. One such consensus protocol, developed by the Quantitative Imaging Biomarkers Alliance (QIBA)[24], is shown below:

Parameter	Compliance levels (for DCE acquisitions)
Pulse sequence	3D fast spoiled gradient recalled echo or equivalent
Coils	Transmit: Body coil
	Receive: Body coil or phased array receive coil dependent on which body part is being studied.
TE	Acceptable: 2.0 – 2.5 ms
	Target: 1.5 – 2.0 ms
	Ideal: < 1.5 ms
TR	Acceptable: 5 – 7 ms
	Target: 3 – 5 ms
	Ideal: < 3 ms
Temporal resolution	< 10 seconds per frame
Flip angle	25° – 35°
Receiver bandwidth	≥ ±31.25 kHz (or ~250 Hz/pixel)
Number of slices	Acceptable: ≥10 prior to zero fill
	Ideal: As many as possible while maintaining ideal temporal resolution.
Slice thickness	Acceptable: 6.1 – 8 mm
	Target: 5.1 – 6 mm
	Ideal: < 5 mm
Matrix	256 x 160 (before applying rectangular FOV)
In-plane spatial resolution	1 – 2 mm
Number of acquisitions (phases)	Sufficient to allow acquisition of at least 5 minutes of post injection data plus at least 5 phases acquired before contrast agent injection (baseline images)

- **Imaging plane:** The acquisition plane should include the lesion or tissue of interest and a *feeding vessel with in-plane flow* in order to capture arterial input function (AIF). In addition, the choice of the acquisition plane should be made, where possible, to mitigate the effects of lesion motion (see section 0).

- **Frequency encoding direction:** The frequency encoding direction should be adjusted so as to minimise motion artefacts. This decision will be based on the location of the lesion or tissue of interest and its relationship to moving structures.

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[24] DCE MRI Technical Committee. DCE MRI quantification profile, quantitative imaging biomarkers alliance. QIBA, 2012.

- **Flip angle:** Flip angles ranging from 25-35 degrees are recommended in order to minimize saturation effects. Smaller flip angles will lead to potential saturation of the signal intensity vs. gadolinium concentration particularly in vessels.
- **T1 mapping:** If a variable flip angle (VFA) series is acquired for pre-contrast agent native T1 mapping, the pulse sequence used for T1 calculation should be the same as used for the DCE protocol and TR/TE values shall stay constant for all flip angles. The number of flip angles varies from typically 2-7 with typically four or more being recommended..

> i
>
> Note that the acquisition requirements shown are specifically developed by QIBA for DCE-MRI acquisition. There may be other consensus protocols that are more optimal for a particular investigation, where the exact sequence parameters used will vary depending on the anatomical or therapeutic area of interest and will involve compromise between coverage, temporal resolution and spatial resolution.

B2. Recommendations on motion control

Motion should ideally be kept to a minimum, which can be achieved through the use of patient positioning aids and/or through optimization of the imaging protocol (including appropriate breathing approaches). Moreover, Dynamika offers a rigid motion correction algorithm (see Section 3) which can correct for movement in-plane. However, deformable motion or motion in a direction orthogonal to the imaging plane is not automatically compensated for.

B3. Scan duration

Dynamika determines the contrast enhancement in each signal intensity curve by comparing the curve to a baseline signal, which is calculated from a number of baseline frames. The baseline frames must therefore be captured before contrast is injected into the subject. Ideally, Dynamika needs at least two to five baseline frames from which to calculate the baseline values.

After the contrast has been injected, if an insufficient number of frames are acquired during the contrast enhancement phase then the full shape of the intensity curve for each pixel will not be captured. It will then be impossible for Dynamika to identify that an intensity curve describes any of the desired shapes (i.e. persistent, plateau or washout). In a normal subject, 4 – 6 minutes is a sufficient amount of time to acquire the full contrast enhancement sequence, including both a baseline period and a contrast enhancement period. It is usually not recommended that scans are performed which span less than 4 minutes.

It is also important that a sufficient number of acquisitions are performed during a scan. Ideally, as many acquisitions as possible should be performed during the scan. The amount of time between acquisitions should not exceed 15 seconds so as to ensure that the shape of the signal intensity curve is accurately represented. It is important to keep the parameters of each scan the same, including maintaining the same amount of time between acquisitions.