CurveBeam, LLC

OssView Bone Fragility Software Instructions for Use

Date of issue: 04 Dec 2023

Revision History

Revision	Release Date	Change Description
1.0	27 Jul 2023	Initial release for OssView Bone Fragility Software v1.5.2
2.0	04 Dec 2023	Added Section 2.11 Clinical Benefits. Added Section 2.12 Measurement Precision Added antivirus and firewall requirements under Section 2.9 Cybersecurity Considerations. Replaced CurveBeam LLC with CurveBeam AI Limited in document footer and trademark information. Improved formatting.

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1. Glossary of Symbols

Symbol	Symbol Title	Description
	Manufacturer	Indicates the medical device manufacturer.
	Country of manufacture	To identify the country of manufacture of products
EC REP	Authorized representative in the European Community/ European Union	Indicates the authorized representative in the European Community/European Union
UDI	Unique Device Identifier	Indicates a carrier that contains Unique Device Identifier information
	Caution	Indicates the need for the user to consult the instructions for use for important, cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself
	Consult instructions for use Consult electronic instructions for use	Indicates the need for the user to consult the instructions for use. ***Note:*** *The e-IFU indicator can be a manufacture's website URL (Annex A/A.15)*
MD	Medical device	Indicates the item is a medical device.
CE	Conformité Européenne	Indicates that a product has been assessed by the manufacturer and deemed to meet EU safety, health, and environmental protection requirements

This box is present when a warning alerts the user to a potential risk that can affect the outcome of the OssView Bone Fragility Software results.

This box is present to provide general observations or information related to procedures, events or practices which are recommended or essential for a successful operation.

2. Device Description

2.1. Indications for Use

The OssView Bone Fragility software is intended to be used as an aid in the clinical assessment of fracture risk in adult women.

The output of the software is a Structural Fragility Score (SFS) report. SFS is a measure of the bone microarchitecture for aiding in assessing fracture risk and monitoring the effect of treatments on patients across time. SFS is calculated from independent measurements of bone microarchitecture, specifically cortical porosity and trabecular density both extracted from a computed tomography (CT) image at the distal radius.

The OssView Bone Fragility Software is limited to use with the cleared Strax HR-pQCT system.

2.2. Compatible Equipment

The OssView Bone Fragility Software is intended to be used with a Computed Tomography (CT) scanner with less than 10 Microsieverts (mSv) per scan.

The compatible Computed Tomography (CT) machine includes:

- Strax HR-pQCT (K170789)

	Please refer to the compatible CT Equipment User Manual to ensure that the CT equipment is calibrated before use.

2.3. Intended Operational Environment

- **Computer or laptop within the healthcare setting**
  OssView Bone Fragility Software by the healthcare professional is used on a desktop or laptop computer. The sources of distractions present in these environments, i.e., surrounding people or noise, mobile phone, or other sources of distractions, can affect the user interaction with the device.

	Bright light (natural or artificial) shining directly on the user's screen can affect the usage of OssView Bone Fragility Software. Therefore, it is the user's responsibility to use OssView Bone Fragility Software in an environment which has appropriate conditions including for lighting.

- **Mobile devices**

	OssView Bone Fragility Software is **NOT** to be used on mobile devices.

2.4. Intended Use

The OssView Bone Fragility software is intended to be used as an aid in the clinical assessment of fracture risk in adult women.

The output of the software is a Structural Fragility Score (SFS) report. SFS is a measure of the bone microarchitecture for aiding in assessing fracture risk and monitoring the effect of treatments on patients across time. SFS is calculated from independent measurements of bone microarchitecture, specifically cortical porosity and trabecular density both extracted from a computed tomography (CT) image at the distal radius.

The OssView Bone Fragility Software is limited to use with the cleared Strax HR-pQCT system.

2.5. Intended Patient Population

OssView Bone Fragility Software is intended for adult women.

2.6. Intended part of the body or type of tissue applied to or interacted with

OssView Bone Fragility Software is a standalone medical device software and does not interact with the patient physically.

	OssView Bone Fragility Software has not been validated for use in scanning areas other than the distal radius.

2.7. Intended Users

The OssView Bone Fragility Software is intended to be used by physicians, CT machine operator, and their support staff, and CurveBeam technical staff. For these intended users, the Instructions for Use addresses any special skills, training or knowledge required to use the device as intended.

	OssView Bone Fragility Software is only to be used by or under the supervision of qualified healthcare professionals, who have completed CurveBeam training in the use of the software.

2.8. Warnings before Use

	Due to security reasons, you will be logged out of a session after 30 minutes of inactivity. After 3 login failures, you will be locked out of the application. Contact Customer Support.

	OssView Bone Fragility Software is compatible with CT images generated by Strax HR-pQCT (K170789).

Before operating the software, all new users of OssView Bone Fragility Software are required to review this User Manual in its entirety. Minor revisions may be made by CurveBeam at any time and without notice.

There shall not be any motion artifacts on the acquired CT images.

CurveBeam warrants the provision of patient data via the online platform will be encrypted and decrypted through Amazon Web Services (AWS).

If any serious incident that has occurred in relation to OssView Bone Fragility Software, it should be reported to CurveBeam or the National Competent Authority (NCA) in the country of occurrence of the incident.

2.9. Cybersecurity Considerations

Report

- Report potential cyber security issues. Users should report to CurveBeam as soon as possible if the medical device appears to have been impacted by a cyber security issue.

Privacy

- Users should be aware of what content they share online, both in public and private forums, particularly relating to personal information.

Authentication

- Avoid reusing the same passphrase across different services, especially if they are registered under the same email address.
- Never share your passphrases with anyone.
- Be aware of your surroundings when using login details in public.
- This device/application should only be used by authorized or registered users.
- In the event the user account is no longer needed, the account should be deactivated.

Network

- Only use trusted connections or a Virtual Private Network (VPN) when accessing an account, as using public Wi-Fi without the use of a VPN increases the risk that your information could become compromised.

Suspicious messaging

- OssView Bone Fragility Software communicates to users via emails. Users should exercise caution and ensure that the email is trusted before acting on any information contained within it. If in doubt, contact the manufacturer or medical professional, don’t use the details or any links in the suspicious message, use contact details that you trust.

Operating system and web browser update

- Regularly updating the computer operating system and Chrome web browser that you use to access the OssView Bone Fragility Software is important because the most up-to-date software will generally be the most secure.

Antivirus and Firewall

- The cloud infrastructure that hosts the OssView website frontend and backend services have the firewall and antivirus software installed to protect against malware and malicious activity.

- Users shall have an antivirus software and firewall installed on the computer that is used to access the OssView. It is recommended that the antivirus software and firewall be set up for auto-updates, so that these are updated automatically, such that the latest version is available for use.

2.10. Customer Support

When the user has questions or encounter errors, they can contact customer support:

Telephone +1 (267) 483 8081
Email techsupport@curvebeamai.com

2.11. Clinical Benefits

The clinical benefits of the OssView Bone Fragility software are listed below:

- The OssView Bone Fragility software is used as an aid in the assessment of fracture risk in non-osteoporotic women. It is able to measure the cortical porosity and trabecular bone microarchitecture deterioration, which is critical for quantifying fracture risk.
- Fragility fractures occur in 1 of every 2 women in their lifetime and 1 of 5 men and result in increased morbidity, mortality, and healthcare costs, thus causing a significant public health burden. Currently, 70-80% of all women that have fragility fractures remain undefined and so, untreated. The SFS device offers a non-invasive and effective method for assessing deterioration in bone microstructure, which is crucial for diagnosing bone fragility, because the deterioration in microstructure weakens the bone out of proportion to the bone loss causing the deterioration, and out of proportion to the modest changes in Bone Mineral Density measured using bone densitometry, that only measures bone mass, not microarchitecture.

2.12. Measurement Precision

The Root Mean Coefficient of Variation (RMSCV) for the OssView SFS calculations has been determined and is approximately 3.32%, which indicates a good reproducibility of the OssView SFS measurements. The RMSCV is calculated to assess the precision of the SFS measurements and is a measure of the relative variability of measurements on the same subjects.

3. Labelling Summary

Information	Description
The measurand and the units in which it is measured	The measurand is the bone microarchitecture of the patient radius bone (wrist). The algorithm separates the cortical from the trabecular compartment to calculate cortical porosity and loss of trabecular bone. The algorithm achieves the separation by analysing both the local and global intracortical structure to measure the concurrent deterioration in cortical porosity and trabecular density relative to their respective means in premenopausal women. SFS is calculated by quantifying the absolute deterioration from young persons and the deterioration of cortical relative to trabecular deterioration. SFS is an index score. The predictive strength of the index is in its ability to assess fracture risk through the concurrent measurement of deterioration of both cortical and trabecular bone. Refer to “5.3.2 Index Calculation” of this IFU for more details.
Algorithm inputs, including any restrictions on input data	The algorithm input is the HR-pQCT (high resolution peripheral quantitative computed tomography) scan of a patient’s radius bone. The scan image needs to be acquired by the Strax HR-pQCT (K170789) using the patient protocol. The image resolution is 0.08 mm * 0.08 mm *0.08 mm. Refer to “5.3 Algorithm Specifications” of this IFU for more details.
Performance specification (the sources of variability affecting the quantitative imaging output)	The major sources of variability affecting the quantitative imaging output are imaging density fluctuation and motion artefact. But both sources are eliminated by following steps. • The Quality Control (QC) phantom is scanned for monitoring the stability of imaging density. The QC phantom is scanned daily. If a deviation of more than 1% on the brightest phantom insert happens, repeat the QC scan. If the QC is out of range after 10 repeated scans, do not scan patients. Contact CurveBeam LLC. • Motion artefact is due to the motion of the patient’s wrist during the scan. If there are motion artefacts, repeat the patient scan and ask the patient to keep still during the scan.
Instructions for image acceptance or quality assurance activities to be performed by the user	The user should follow the Strax HR-pQCT user manual for image acquisition. • The Strax HR-pQCT Quality Control (QC) phantom is scanned daily for monitoring the stability of imaging density. • Repeat the patient scan if there are motion artefacts.

Qualifications and training needed for a user to be within the device's intended user population	The OssView Bone Fragility Software is intended to be used by physicians, CT machine operator, and their support staff, and CurveBeam technical staff. For these intended users, the Instructions for Use addresses any special skills, training or knowledge required to use the device as intended. OssView Bone Fragility Software is only to be used by or under the supervision of qualified healthcare professionals, who have completed CurveBeam training in the use of the software.
Reference database	A SFS score ≥ 70, identifies women with severe microarchitectural deterioration while women with minimal microarchitectural deterioration have a SFS <70. The risk cut-off was established from a reference database of 324 healthy ambulant premenopausal white women aged 20 – 40 years old in Melbourne, Australia.

4. Product Label

The product label for OssView Bone Fragility Software.

OssView Bone Fragility Software

	CurveBeam, LLC 2800 Bronze Dr., Suite 110 Hatfield, PA 19440 USA www.curvebeamai.com
AU	2023-04-26
EC REP	EA-Services 16 Rue des Sallières 31210 Montréjeau
UDI	(01) 00860004550044 (11) 230426 (8012) 1.5.2
MD	CE 2862

5. System Requirements

5.1. Internet Connection and a browser

OssView Bone Fragility Software requires an internet connection and a browser to be accessed.

⚠	OssView Bone Fragility Software can be accessed via a browser. The following browsers are recommended as they have been validated: Google Chrome version 83 or newer

Chrome browser on Windows
To use Chrome browser on Windows, the user will need:

Windows 10 or later
An Intel Pentium 4 processor or later that is SSE3 capable.

Chrome browser on Mac
To use Chrome browser on Mac, the user will need:
macOS 11 or later

Chrome browser on Linux
To use Chrome browser on Linux, the user will need:

64-bit Ubuntu 20.04+, Debian 11+, openSUSE 15.4+, or Fedora Linux 36+
An Intel Pentium 4 processor or later that is SSE3 capable.

5.2. Installation

OssView Bone Fragility Software does not require installation by the user, only a supported browser is required.

5.3. Firewall

If the internet access of the user is behind a firewall, the OssView Bone Fragility Software domain will have to be whitelisted.

⚠	If the user cannot access the OssView Bone Fragility Software (e.g., firewall on user's device or network) the user will need to contact Customer Support.

5.4. Operational security options

There are no operational security options to be set at installation time.

5.5. Decommission and disposal of OssView Bone Fragility Software

For safe decommission and disposal of your data, please contact Customer Support.

5.6. Viewing OssView Bone Fragility Software analysis report

When the CT images have finished uploaded to the OssView Bone Fragility Software and analysis is completed, OssView Bone Fragility Software will generate an analysis report of the Structural Fragility Score (SFS).

⚠ For viewing OssView Bone Fragility Software analysis reports, the user can use any PDF viewer installed on the user's device.

5.7. Image Requirements

OssView Bone Fragility Software is compatible with CT images generated by Strax HR-pQCT (K170789).

⚠ OssView Bone Fragility Software supports DICOM image data, with a spatial resolution between 100-120 microns. No other type of imaging is supported.

⚠ There shall not be any motion artifacts on the CT image generated.

5.8. Error Handling

In cases where the user encounters errors with accessing OssView Bone Fragility Software, consult the following list and follow the error resolution guidelines.

Error type	OssView Bone Fragility Software on the user's device/system does not work temporarily.
Resolution	The user needs to close the tab/browser and re-open OssView Bone Fragility Software. If the error persists, the user should contact Customer Support.

Error type	The user is unable to access OssView Bone Fragility Software.
Resolution	The user should contact Customer Support.

6. OssView Bone Fragility Software User Manual

6.1. General Aspects

6.1.1. Introduction

All new users of OssView Bone Fragility Software are required to review this User Manual in its entirety. Experienced users can use this user manual to consult the sections they require. Improvements and changes to this user manual necessitated by typographical errors, inaccuracies of current information, or improvements to programs/equipment may be made by CurveBeam at any time and without notice. This manual is published by CurveBeam without any warranty.

6.1.2. Accessibility

The following items can be scaled using zoom options of the browser and/or PDF viewer:

- OssView Bone Fragility Software application
- OssView Bone Fragility Software analysis report
- Product Label
- Instructions for Use

6.1.3. Information Security

CurveBeam warrants that the provision of image data via the online platform will occur via an encrypted connection and that this transfer will meet the highest safety standards. Image data uploaded to Amazon Web Services (AWS) will be de-identified before use in the OssView Bone Fragility Software web environment.

6.2. OssView Bone Fragility Software Application

6.2.1. Account Creation

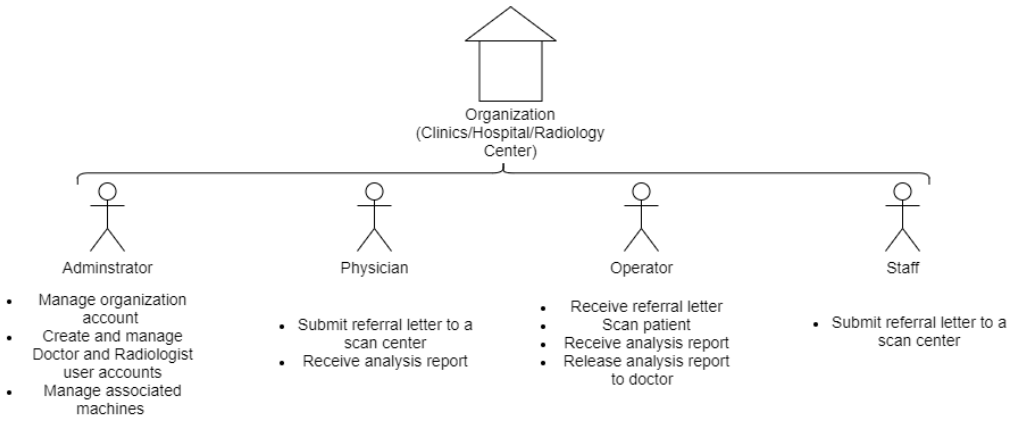


Fig. 1: Organization and Users

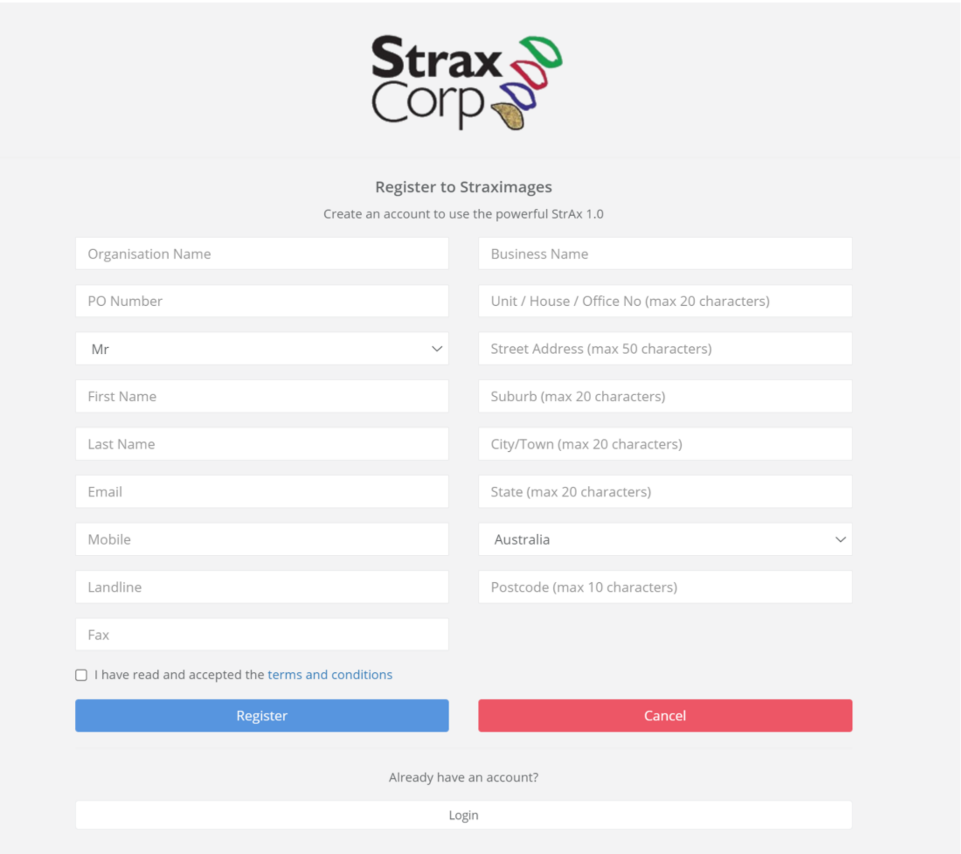
To use OssView Bone Fragility Software, physician, staff, and operator user accounts need to be created.

Staff user is a special user that is created to assist physicians with patient management. The staff user from the same physician location can add, edit, look, and search patients. They can also submit referrals on behalf of the physicians.

The relationship chart of user accounts is shown in Fig. 1. Physician, staff, and operator user accounts are created and managed under an organization. An organization could be a clinic, hospital, or scanning centre. The administrator user account is the managing account of the organization. The administrator user registers an organization through the OssView Bone Fragility Software's web system and then creates physician, staff, and operator user accounts. The organization registration and user account creation are demonstrated with the screenshots as follows:

1. Go to https://www.ossview.com, fill out the registration form to register an organization. The administrator user completes the registration form. The user information (name, email, mobile) is the administrator user's information.

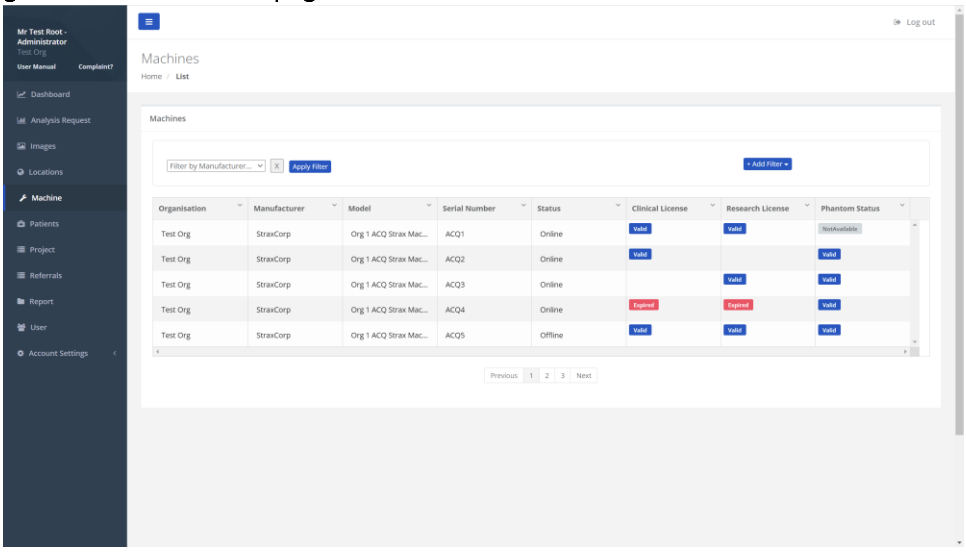
   Please note, as explained above, this form is only for organization and organization administrator user registration. Physician, staff, or operator user accounts need to be created by the administrator user under an organization.



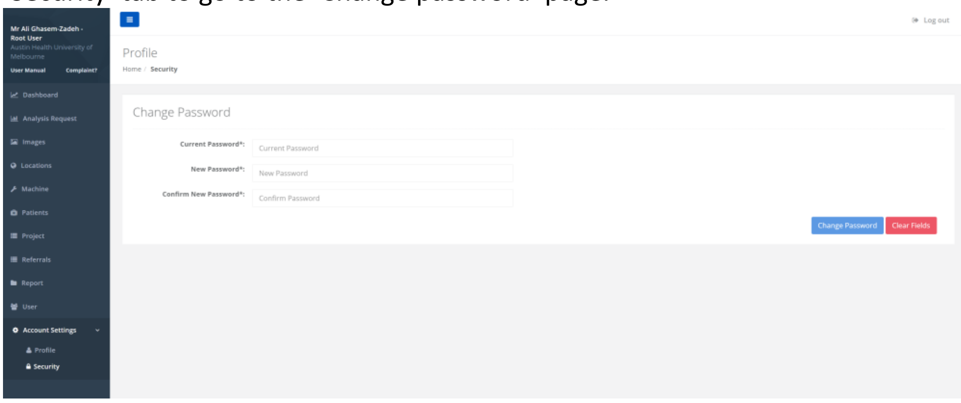
2. CurveBeam validates and approves the registration. Once the registration is approved, the organization is registered, and the administrator user account of the organization is created in the OssView Bone Fragility Software's system.

3. Once the registration is approved, CurveBeam sends a confirmation email with the login password to the email address supplied on the registration form. The administrator user goes to https://www.ossview.com/#/login and uses the email address and password to log in.

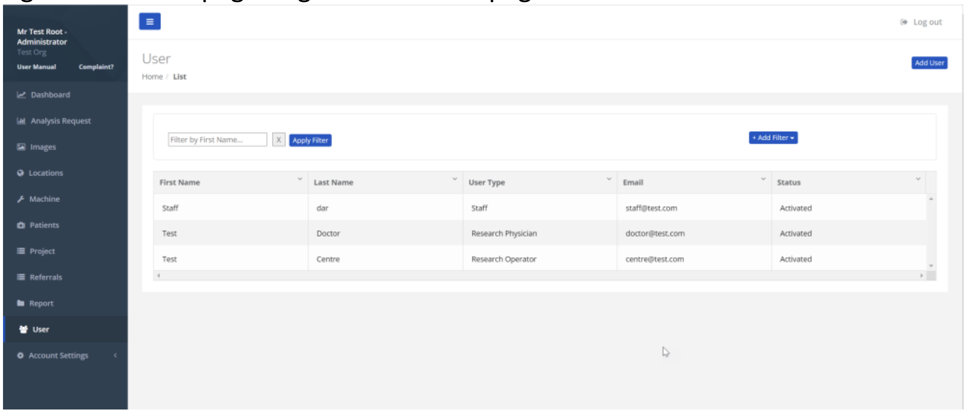
4. After the organization is registered, CurveBeam will add one or more CT scanners to the organization account according to the contract between CurveBeam and the organization. After the machine is added, the administrator user can see the 'Machine' tab in the module-navigation panel on the left which when clicked on goes to the Machine's page.



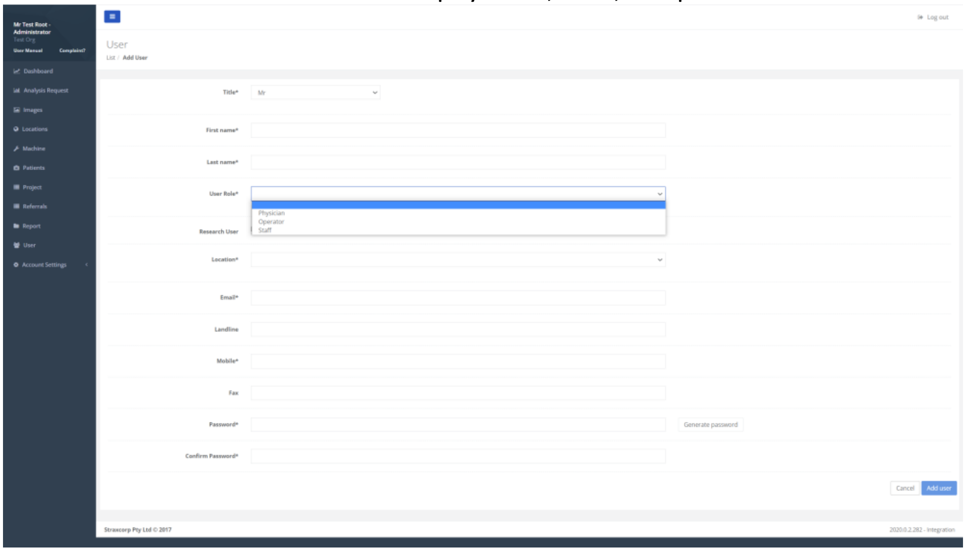
5. Once the administrator user logs in, the user can change the password in the 'Account Setting/Security' module. The administrator user clicks the 'Account Settings' menu tab on the module-navigation panel on the left, then clicks the 'Security' tab to go to the 'Change password' page.



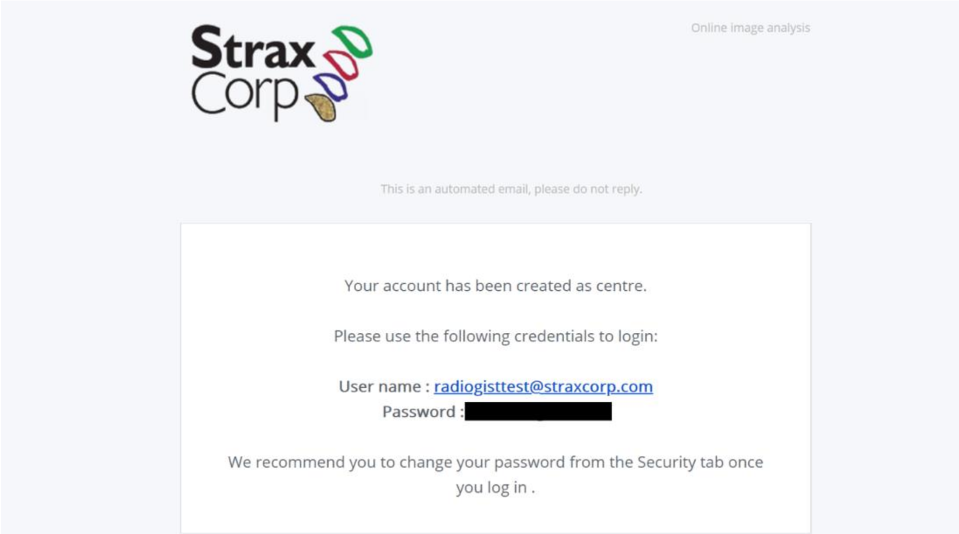
6. The administrator user of the organization creates a physician, staff, or operator user account in the ‘User’ module. The administrator user clicks the ‘User’ tab on the module-navigation panel on the left, then clicks the ‘Add User’ button on the right of the web page to go to the ‘User’ page.



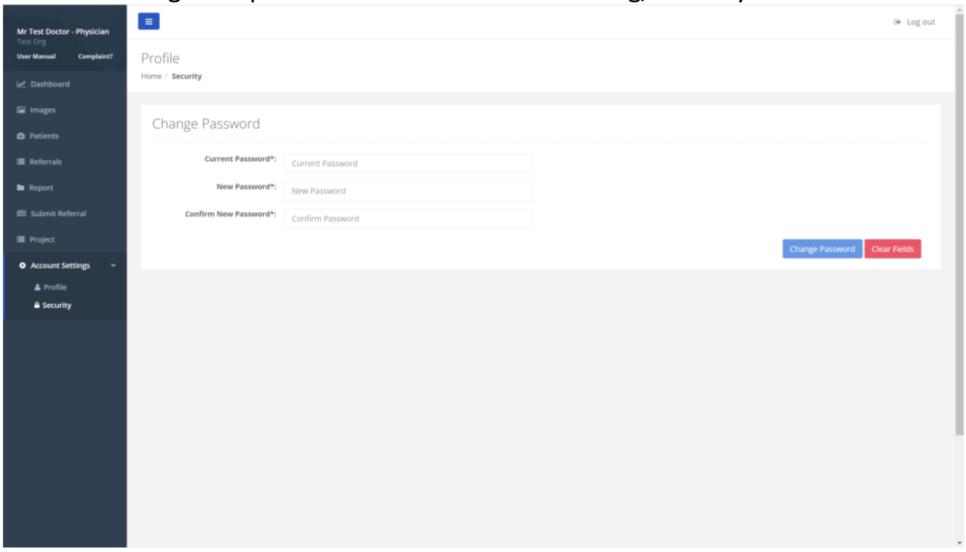
7. The administrator user fills out the form on the ‘Add User’ page to create a physician, staff, or operator user account. The administrator user selects ‘Physician’, ‘Staff’ or ‘Operator’ in the ‘User role’ drop-down menu to create a physician, staff, or operator account; fills out the email address of the physician, staff, or operator in the textbox of ‘Email’; fills out or generates an initial password in the text box of ‘Password’ for the physician, staff, or operator user.



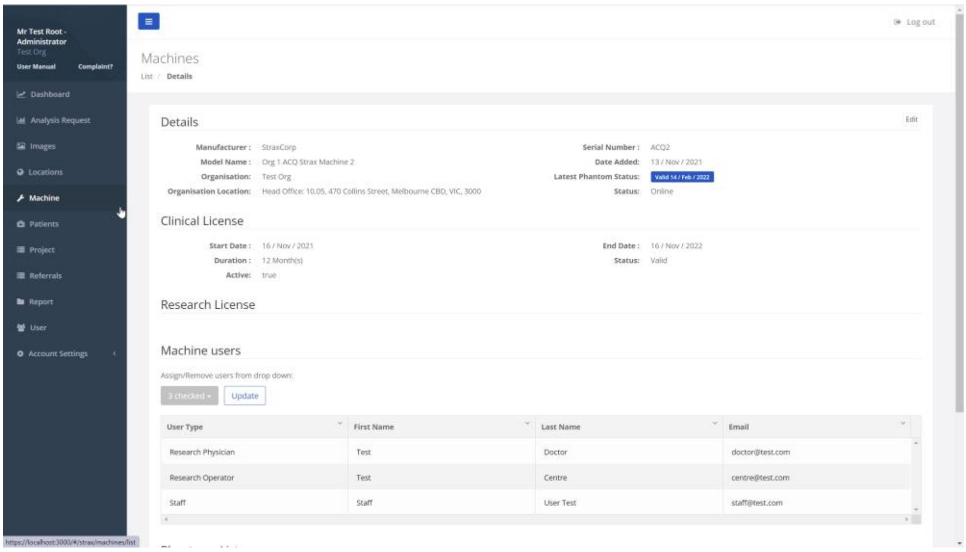
8. After completing the form, the administrator user clicks the ‘Add user’ button at the bottom left of the page. The ‘Add user’ form is submitted, and the user account is created. The physician, staff or operator receives an automated email from CurveBeam with the login credential.



9. The physician, staff or operator goes to https://www.ossview.com and logs into the account using the account credentials in the email. After the initial login, the user can change the password in the ‘Account Setting/Security’ module.



10. Once an operator user account is created, the administrator user needs to add the operator user to the machine. The administrator user clicks the ‘Machine’ tab in the module-navigation panel on the left to go to the ‘Machine’ page; clicks the machine row in the ‘Machines’ list to go the ‘Machine detail’ page. In the ‘Machine user’ section, click the ‘Check’ drop-down menu to ‘Check’ or ‘Uncheck’ a user for adding or removing a user to or from the machine. Check the operator user and click the ‘Update’ button next to the ‘Check’ button. After the ‘Update’ button is clicked, the administrator user sees the operator user in the ‘Machine user’ list.



6.2.2. Patient Workflow

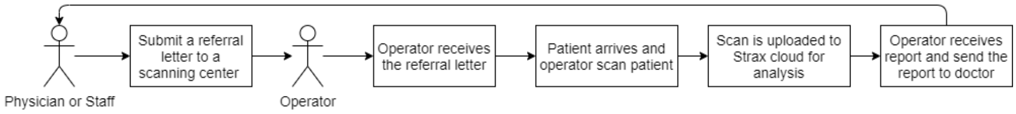


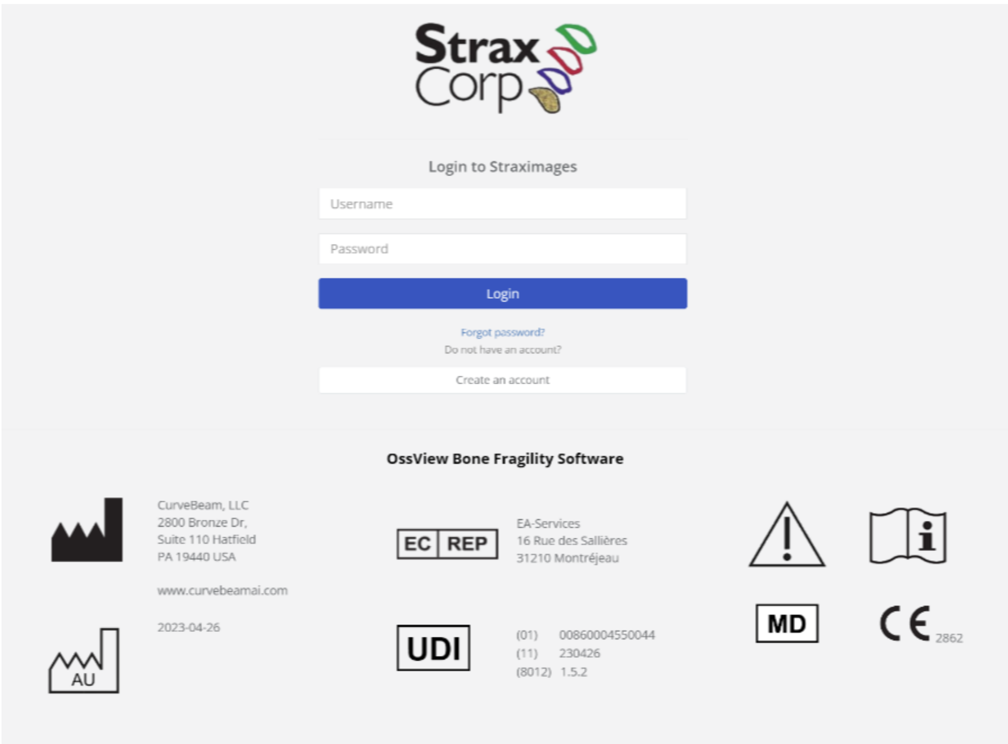
Fig. 1: Patient Workflow

The patient workflow is the procedure from the submission of a referral letter for a patient to a scanning centre to receive the OssView Bone Fragility Software's analysis report of the patient's wrist scan. The patient workflow is shown in Fig. 2.

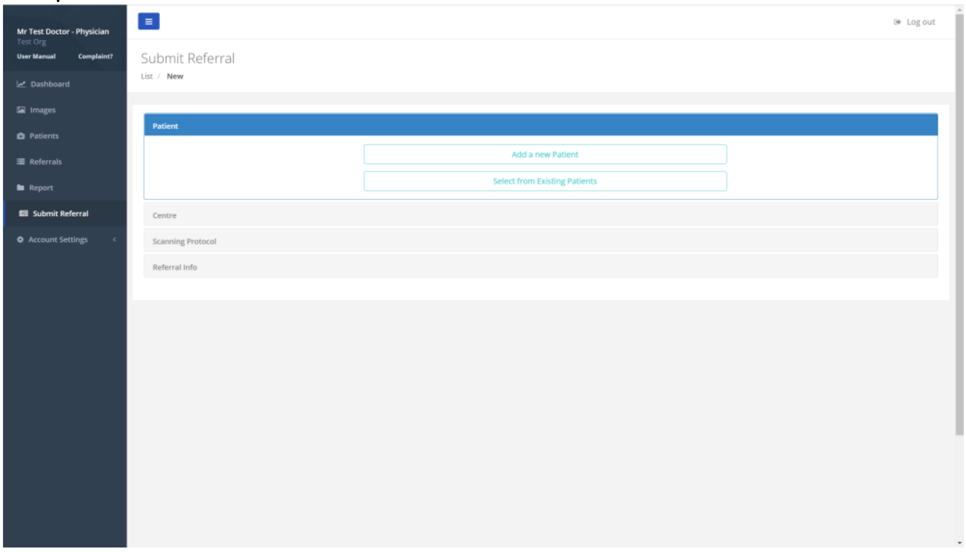
A physician or staff user sees a patient and submits a referral letter for the SFS test to a scanning centre. The operator receives the referral letter. The patient arrives at the scanning centre. The operator has to confirm with the patient that the patient's details (e.g., first name, last name, date of birth) on the referral are correct. The operator scans the patient's wrist with the correct laterality (i.e., left wrist or right wrist). After the scan, the wrist scan is uploaded through the OssView Bone Fragility Software's web system for SFS analysis.

The operator receives the SFS analysis report and sends it to the physician. The physician receives the analysis report provides the results to the patient. The key steps of the patient workflow are demonstrated with the screenshots as follows:

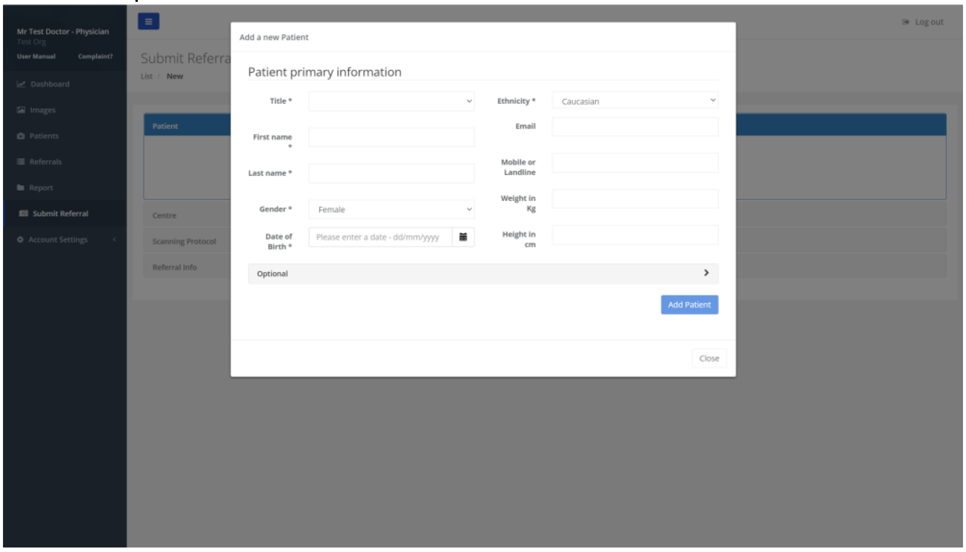
1. A physician or staff user goes to https://www.ossview.com/#/login and logs in to the physician or staff account.



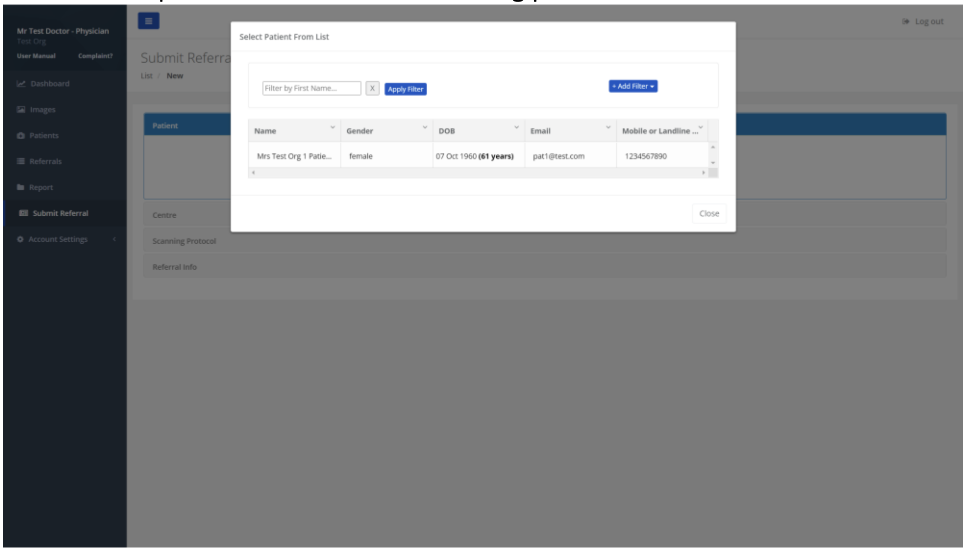
2. The physician or staff user creates and submits a referral letter in the 'Submit Referral' module. The physician or staff user clicks the 'Submit Referral' tab on the module-navigation panel to go to the 'Submit Referral' page. There are four sections on the 'Submit Referral' page: 'Patient', 'Centre', 'Scanning Protocol', and 'Referral Info'. The physician or staff user completes the four sections to submit a referral letter. One section will be displayed after the previous section is completed.



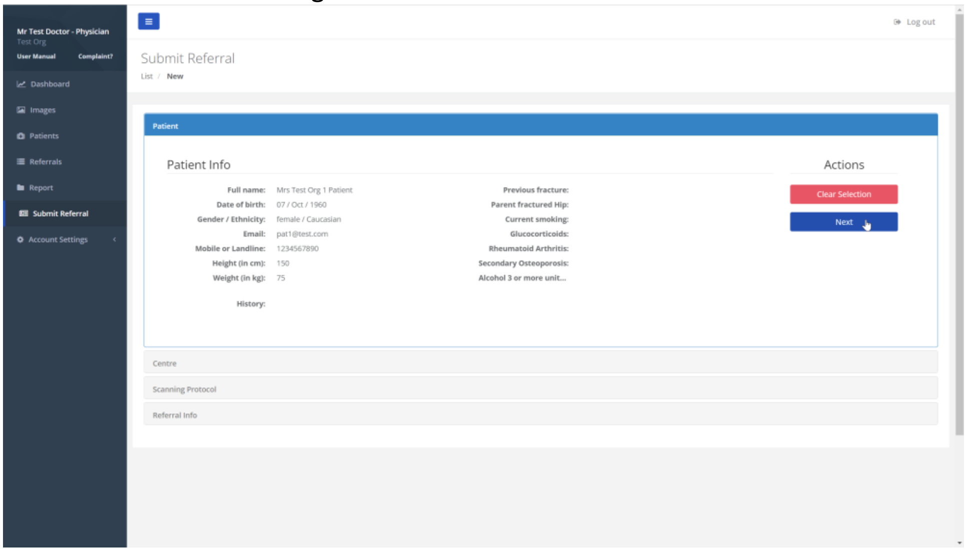
3. In the 'Patient' section, the physician or staff user fills out the patient information. If the patient information has not been added to the OssView Bone Fragility Software before, the physician or staff user clicks the 'Add a new Patient' button to add the patient information.



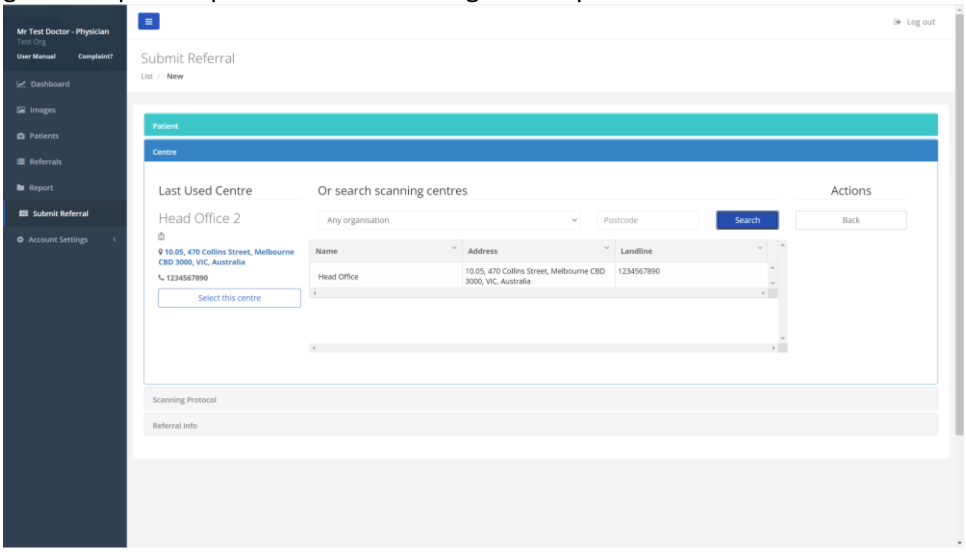
4. If the patient information was added to the OssView Bone Fragility Software before, the physician or staff user clicks the ‘Select from Existing Patients’ button to select the patient from the list of existing patients.



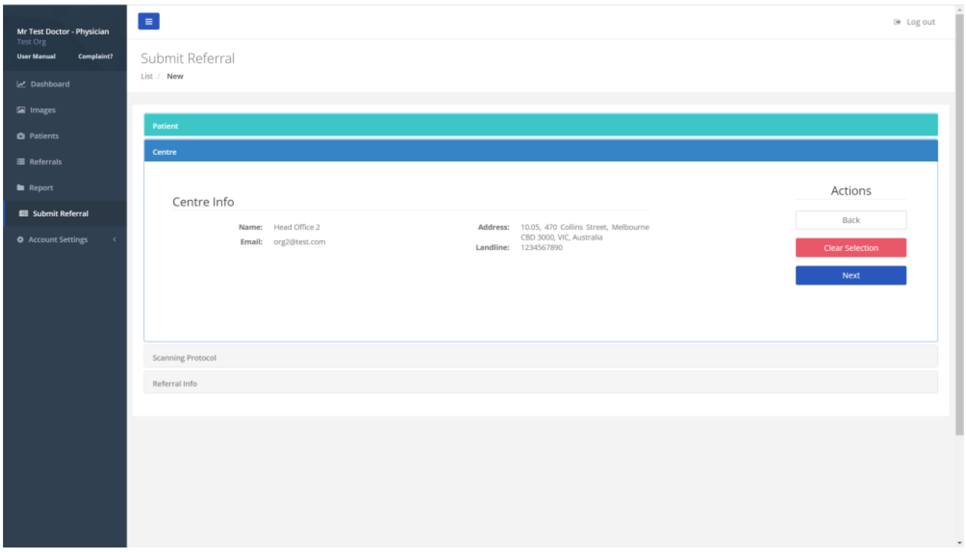
5. Once the ‘Patient’ section is complete, the physician or staff user clicks the ‘Next’ button under ‘Actions’ to go to the ‘Centre’ section.



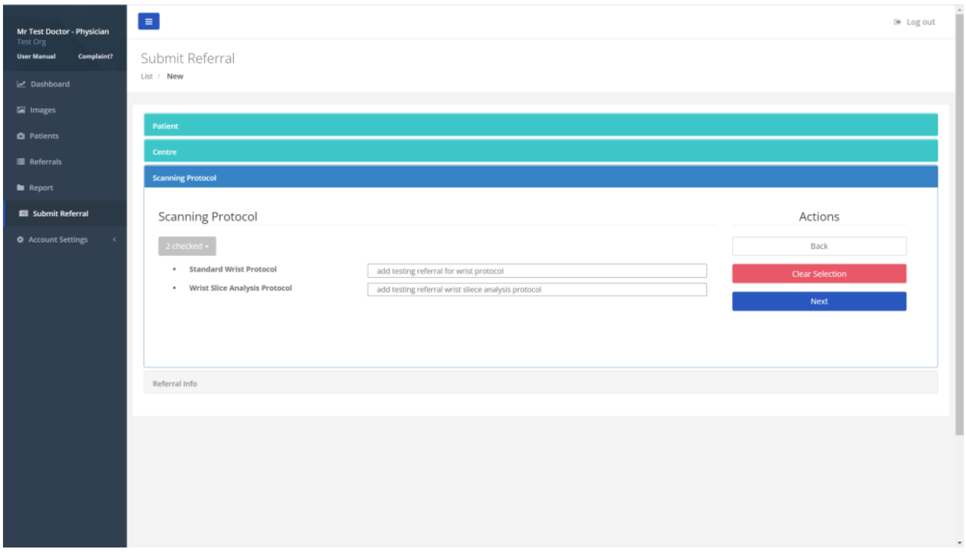
6. In the ‘Centre’ section, the physician or staff user selects the scanning centre. The physician or staff user can either select the centre used last time or search for a new scanning centre. The physician or staff user can click on the ‘Back’ button to go to the patient panel to make a change in the patient selection.



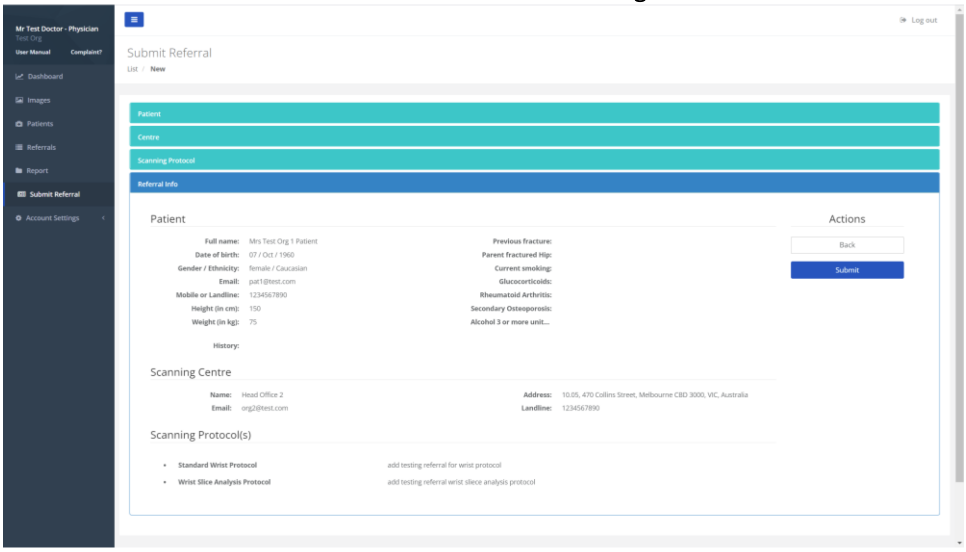
7. Once the ‘Centre’ section is complete, the physician or staff user clicks the ‘Next’ button under ‘Actions’ to go to the ‘Scanning Protocol’ section. The physician or staff user can click the ‘Clear Selection’ button to undo the centre selected.



8. In the ‘Scanning Protocol’ section, a list of scanning protocols associated with the machine license are shown in the drop-down list. The physician or staff user can click on the ‘Back’ button to go back and make changes to the centre selection. The physician or staff user can click the ‘Next’ button under ‘Actions’ to go to the ‘Referral Info’ section.



9. In the ‘Referral info’ section, the information from the referral letter is displayed for the physician or staff user’s review. If the information is correct, the physician or staff user clicks the ‘Submit’ button under ‘Actions’ to submit the referral letter to the scanning centre; if the information is incorrect, the physician or staff user clicks the ‘Back’ button under ‘Actions’ to make changes.



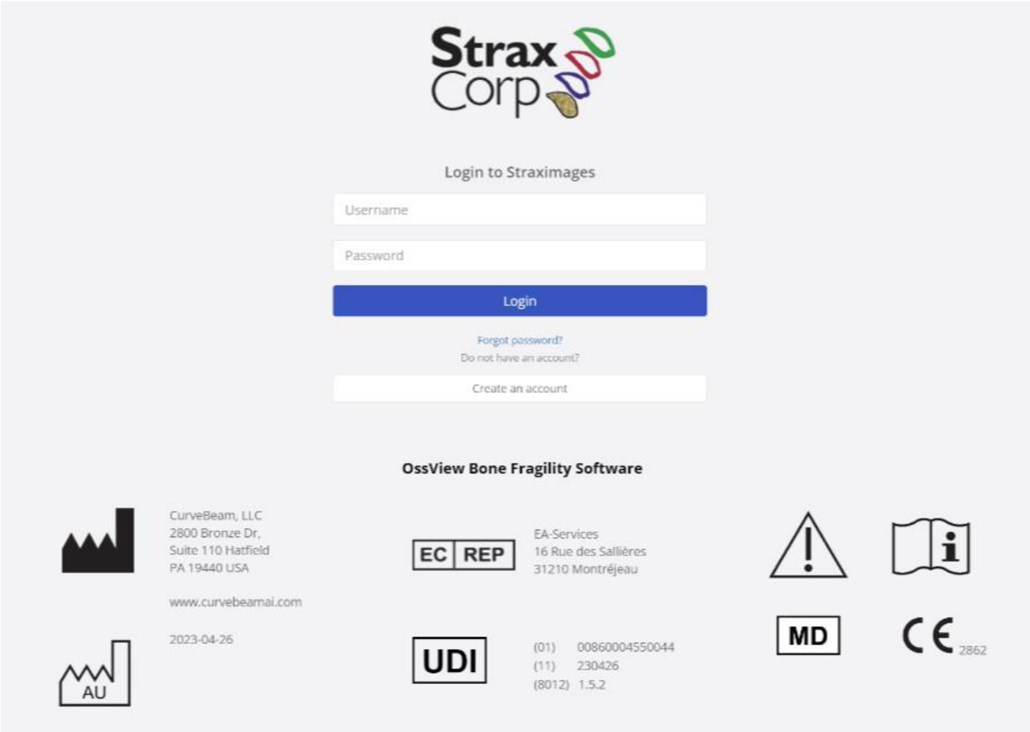
10. The referral letter is submitted to a scanning centre. The patient goes to the scanning centre. The operator must confirm that patient details with the patient, confirm the laterality of the patient to be scanned, then scan the patient’s wrist and upload the scan through the OssView Bone Fragility Software’s website for the analysis. Please refer to CT Scan Upload Workflow for more detail.

11. Once the analysis is complete, the operator receives the report. The operator reviews the report and sends it to the physician who requested the referral letter. Please refer to Report Release Workflow for more detail.

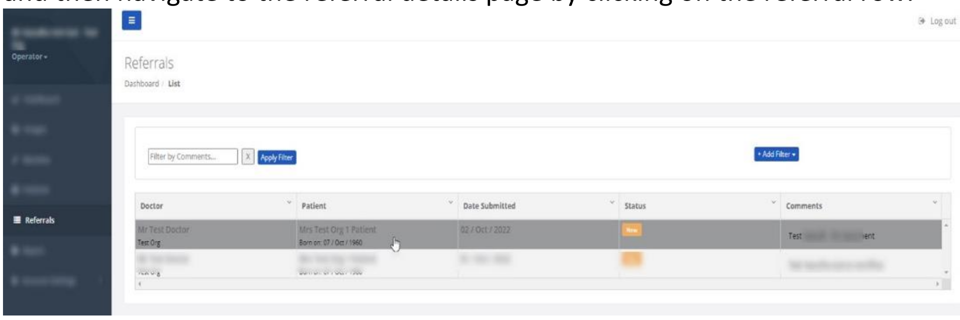
6.2.3. CT Scan Upload Workflow

The CT scan images of the patient's wrist need to be uploaded via the web application portal.

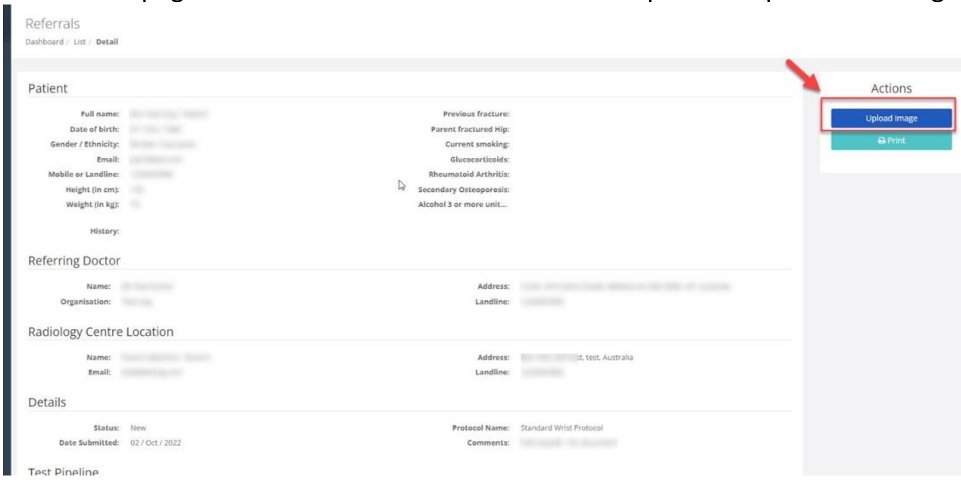
1. An operator user goes to the [https://www.ossview.com/ - /login](https://www.ossview.com/#/login) page and logs into the operator account. Please refer to the 'Account Creation' section for the operator user account creation.



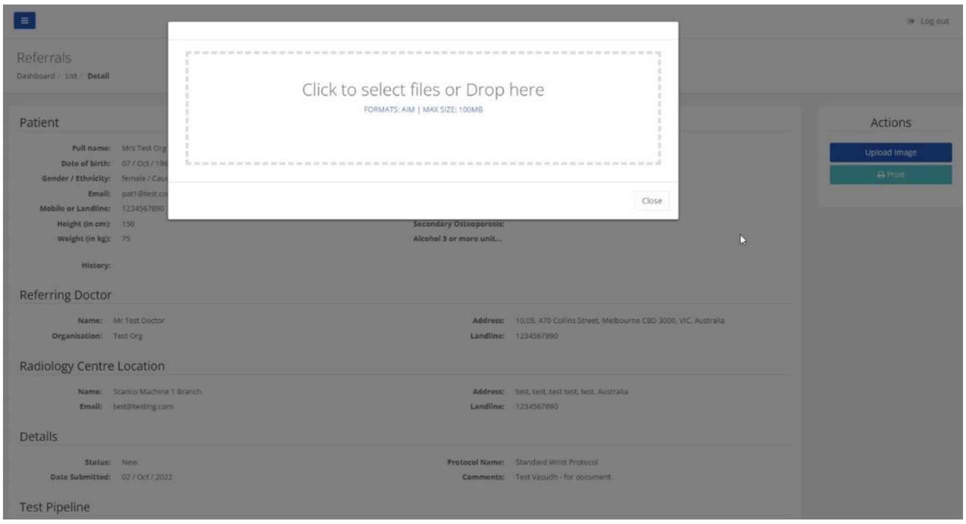
2. The operator clicks the 'Referrals' tab and should be able to see the referrals list, and then navigate to the referral details page by clicking on the referral row.



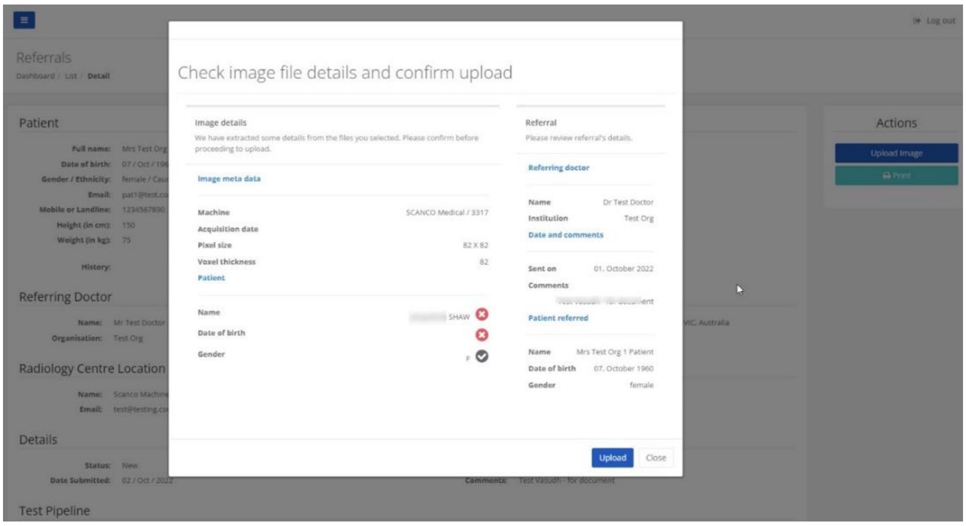
3. The details page will be as shown as below with the option to upload the image.



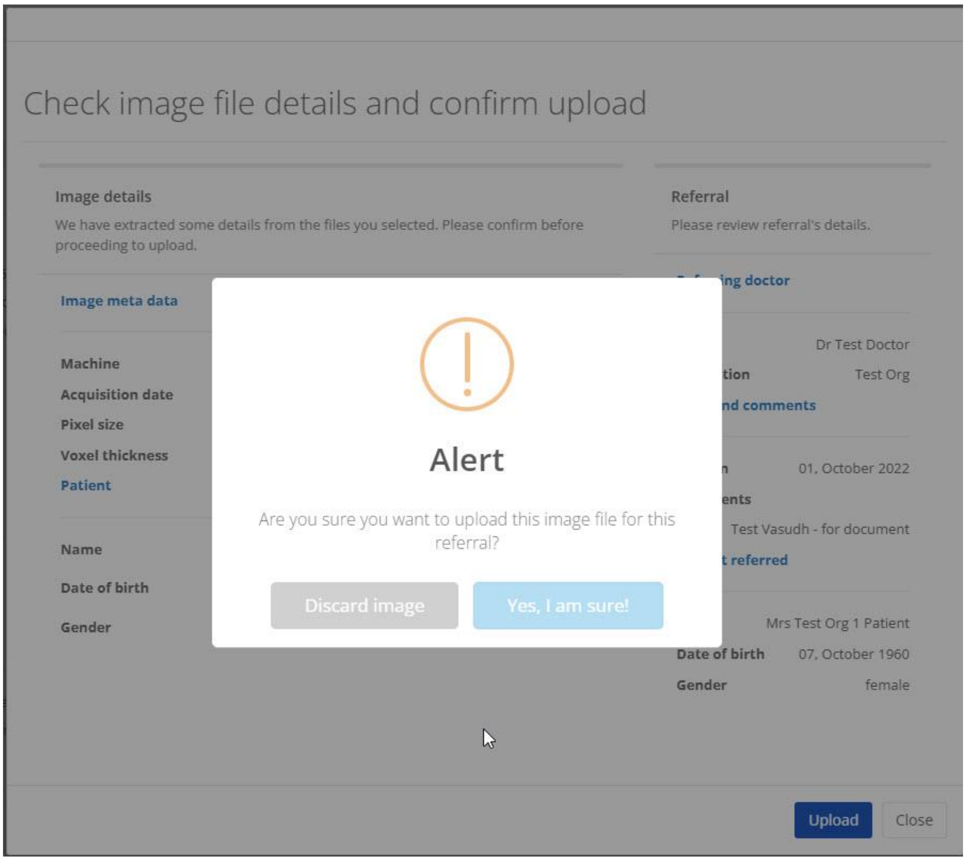
4. When the operator user clicks on 'Upload Image' button, the upload option will pop up as shown below where the user needs to drop/select the files to upload. The supported image formats are AIM.



5. When the image is dropped/selected on the upload page, the patient data is extracted from image header and is displayed on the page for the user to verify the data against the referral data.



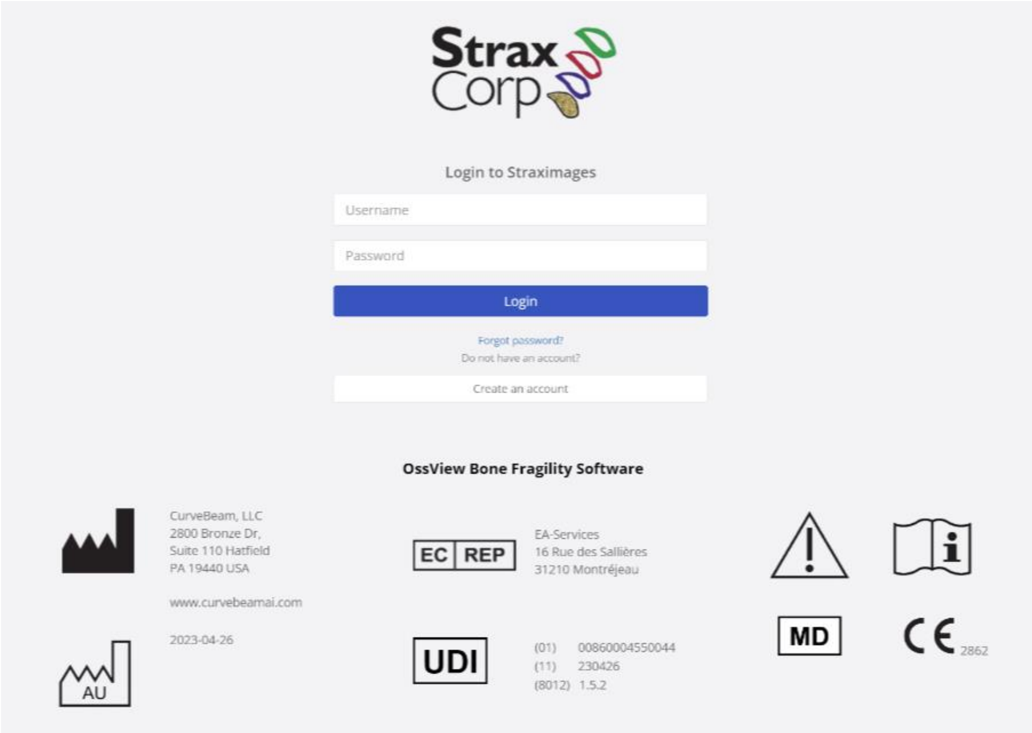
6. If the patient data in the image does not match the patient data in the referral, a warning message will be shown, and options will be given to the user to either 'Discard' or 'Upload' the image.



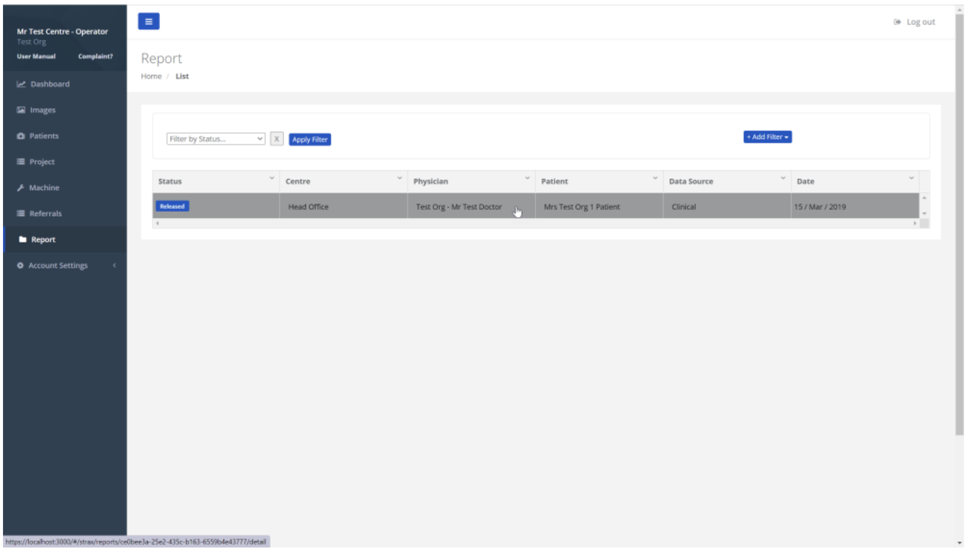
7. If the operator is sure about the patient details, they can proceed to upload the image by clicking 'Yes, I am sure!' button. The image will be uploaded for analysis once the user confirms the upload.

6.2.4. Report Release Workflow

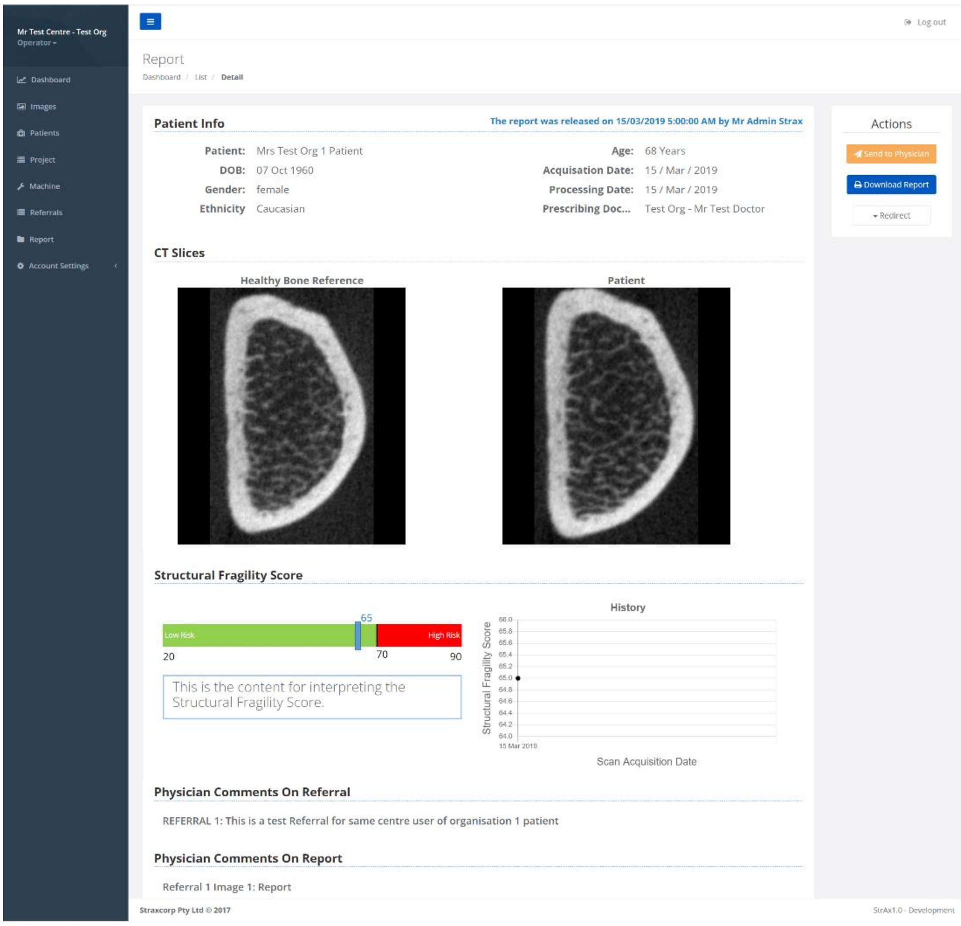
1. Once the analysis is complete, the operator receives the report. The operator goes to https://www.ossview.com/#/login and logs in to the operator account. Please refer to the Account Creation for the operator user account creation.



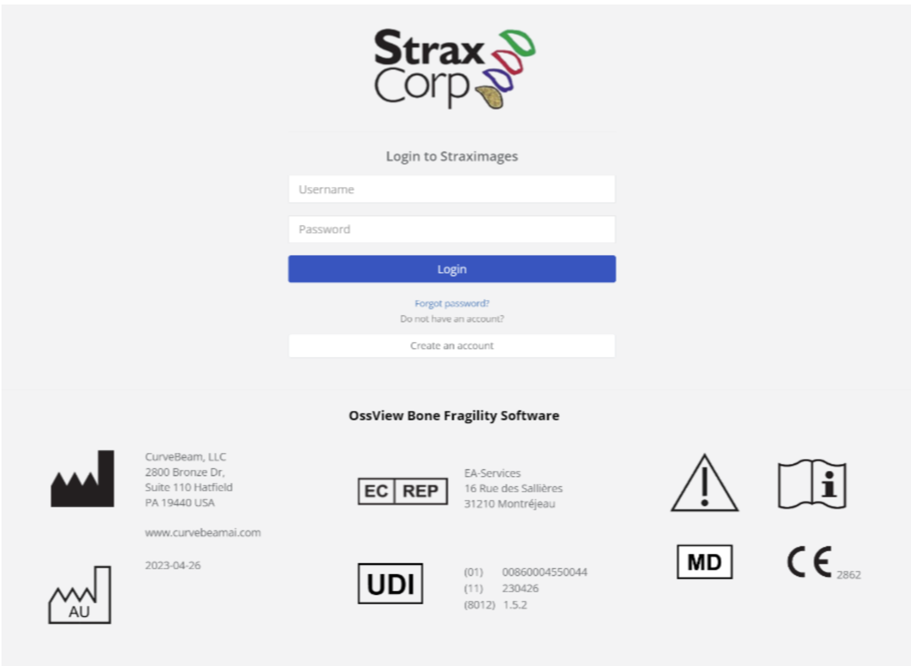
2. The operator clicks the 'Report' tab on the module-navigation panel to go to the 'Report' page.



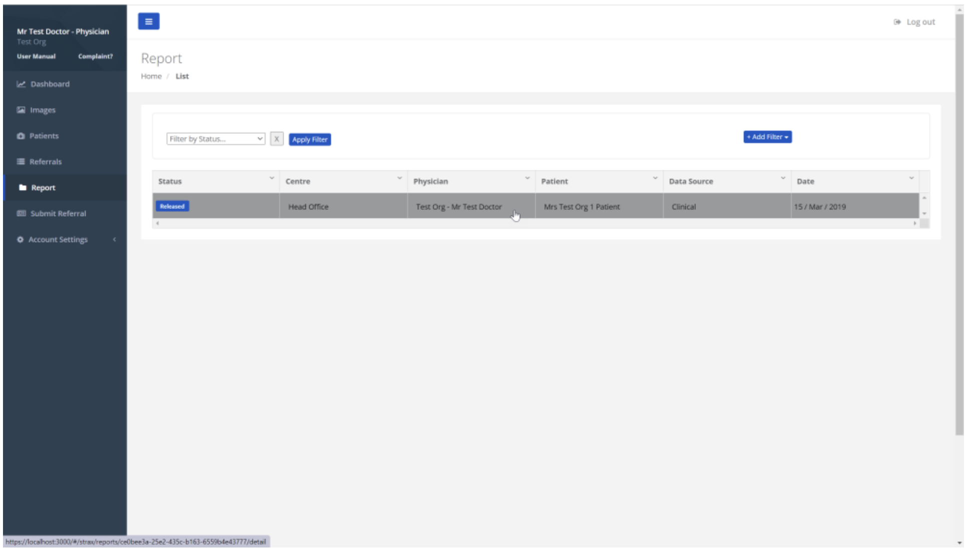
3. The operator clicks a row in the report list to go the page of the report detail. The operator clicks the ‘Send to Physician’ button under ‘Actions’ to the physician or staff user who requested the referral.



4. The physician or staff user goes to https://www.ossview.com/#/login and logs in to the physician account.



5. The physician or staff user receives the report. The physician clicks the ‘Report’ tab on the module-navigation panel to go to the ‘Report’ page.



6. The physician or staff user clicks a row in the report list to go to the page of the report detail.

Ossview 1.5.2 Analysis of Bone Microstructure Report

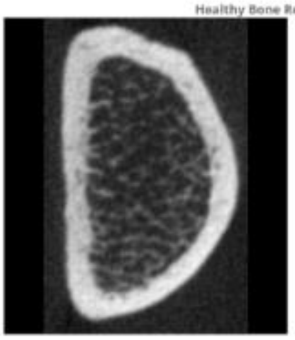
Patient Info

Patient: Mrs Test Org 1 Patient
DOB: 07 Oct 1960
Gender: female
Ethnicity Caucasian

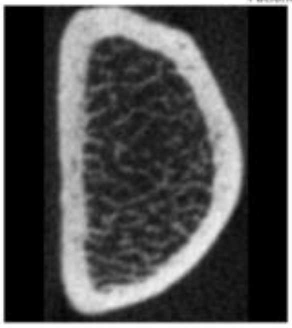
Age: 68 Years
Acquisation Date: 15 / Mar / 2019
Processing Date: 15 / Mar / 2019
Prescribing Docto Test Org - Mr Test Doctor

CT Slices

Healthy Bone Reference



Patient



Structural Fragility Score

This is the content for interpreting the Structural Fragility Score.

History

Physician Comments On Referral

REFERRAL 1: This is a test Referral for same centre user of organisation 1 patient

Physician Comments On Report

Referral 1 Image 1: Report

Device label

OssView Bone Fragility Software

CurveBeam, LLC
2800 Bronze Dr.
Suite 110 Hatfield
PA 19440 USA

www.curvebeamai.com

AU 2023-04-26

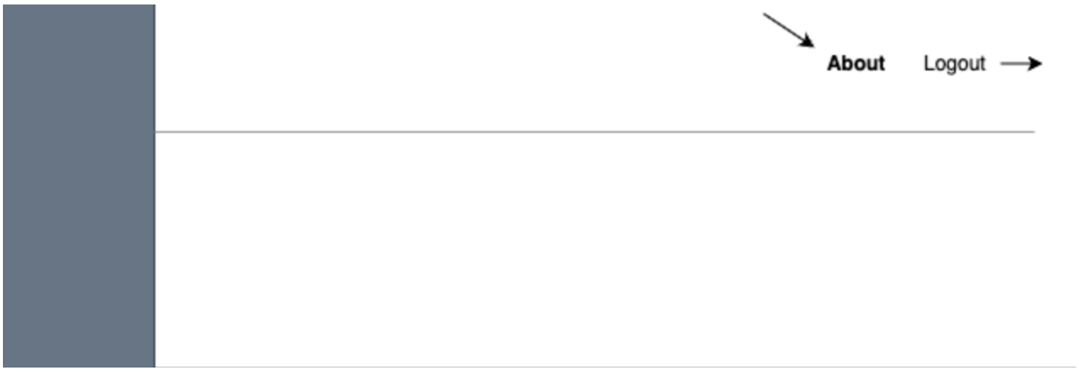
EC REP EA Services
16 Rue des Salières
31210 Montréjeau

UDI (01)
(11) 230426
(8012) 1.5.2

MD CE

6.2.5. About

The About button will open the product label of OssView Bone Fragility Software on the screen.



6.2.6. Interpretation of Structural Fragility Score

The Structural Fragility Score is depicted as an indicator bar. The SFS indicator bar indicates the following:

- Low risk (green region) below the Fragility Risk Threshold
- High risk (red region) above the Fragility Risk Threshold

The SFS value should display in SFS history graph (beside the SFS indicator bar) which shows the patient's SFS in the follow-up scans against the follow-up dates.

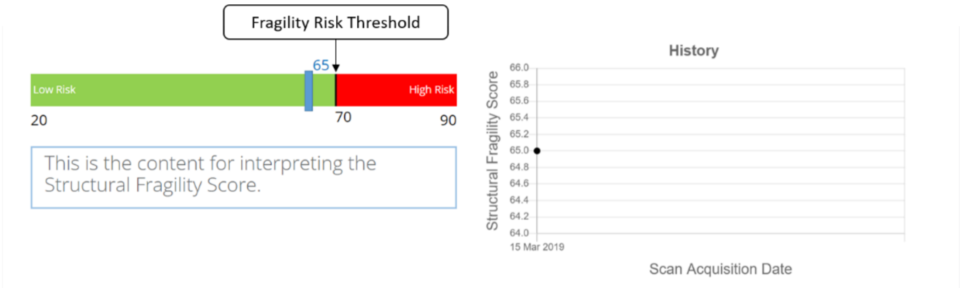


Fig. 3: SFS indicator bar and history graph

6.3. Algorithm Specifications

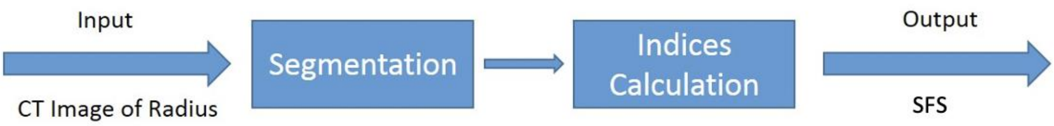


Fig. 4: Image Analysis Overview

By referring to figure above, image analysis unit consists of two steps: segmentation and indices calculation. In the first step, the structure of the radius bone on the loaded image will be identified. First, the entire bone will be segmented from the soft tissue. Subsequently, the entire bone will be segmented into four compartments: hard cortex, outer transitional zone, inner transitional zone, and trabecular compartment. In the second step, the three parameters will be calculated based on the bone structure. The whole procedure of image analysis is automatic without manual intervention.

6.3.1. Segmentation

The segmentation is achieved by automatically selecting attenuation profile curves perpendicular to the periosteal surface. Local bone edges are identified as the beginning and the end of the rising and falling S-shaped portions of the curve.

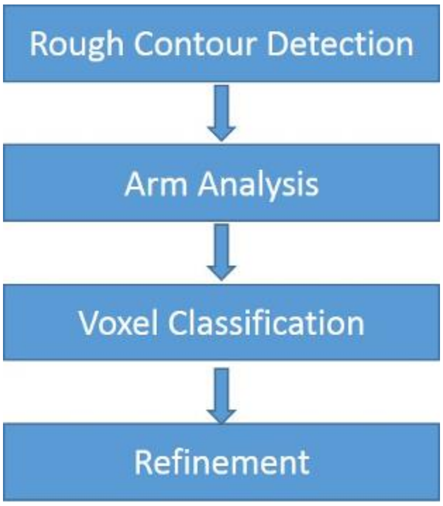


Fig. 5: Segmentation Process

As shown in Fig. 5, external contour of the entire bone is identified roughly at the beginning. Subsequently, consecutive overlapping profiles of attenuation in rectangular region of interests (ROI's) along the external contour are generated and analysed. We refer to this ROI as an arm. Bone tissues in each arm will be classified into four different compartments: hard cortex, outer transitional zone, inner transitional zone, and trabecular compartment. The classification of each voxel will be accumulated during analysis of all the arms. The arm rotates along the rough external contour ensures that every voxel is reanalysed many times. For an HR-pQCT image of the distal radius, a voxel may reappear in several hundred overlapping arms. Ultimately, each voxel location is attributed to the compartment in which it has appeared the maximum number of times. This multi-categorisation of voxel location minimises segmentation errors and is an essential feature of this ''edge finder' algorithm. After arm analysis, internal and external refinement will be implemented for optimising the segmentation. The segmentation procedure will be applied on all the cross-section slices. The design of rough external contour identification, arm analysis, and refinement will be presented in detail as following.

6.3.1.1. Rough External Contour Identification

Identifying the rough external contour of the radius bone is the first step of segmentation. The input image is first binarised into foreground (bone) and background (soft tissue). All foreground voxels will be connected as blobs and all the contours of these blobs are detected. The longest contour is selected as the rough external contour. Because external contour is critical for generating arms, a correction algorithm is implemented to optimise the contour based on the morphologic attributes of radius bone.

6.3.1.2. Binarisation

The binarisation step converts the input image into a white-and-black image. The foreground (white) is the bone while the background (black) is soft tissue. The maximum entropy threshold [2] is utilised in this step. It does automatic thresholding based on the entropy of the histogram. Entropy is a measure of the uncertainty of an event taking place. By maximising the inter-class entropy, the threshold value is selected. The entropy [S] is calculated as:

$$S = -(sum)p * log2(p) \quad (1)$$

where p is the probability of a voxel greyscale value in the image, and (sum) is the Greek capital sigma. It is customary to use log in base 2.

6.3.1.3. Contour Detection

Contours are detected on the binary image by applying the algorithm in [3]. The algorithm proposed a topological analysis with border following. Border following derives a sequence of the coordinates or the chain codes from the border between a connected component of foreground and a connected component of background. The algorithm determines the relations among the borders of a binary image. Since the outer borders and the "hole" borders have a one-to-one correspondence to the connected components of foreground and to the background, respectively, the algorithm extracts the topological representation of a binary image. After all the contours of foreground are detected, we select the longest contour as the rough external contour the bone.

6.3.1.4. Correct Contour

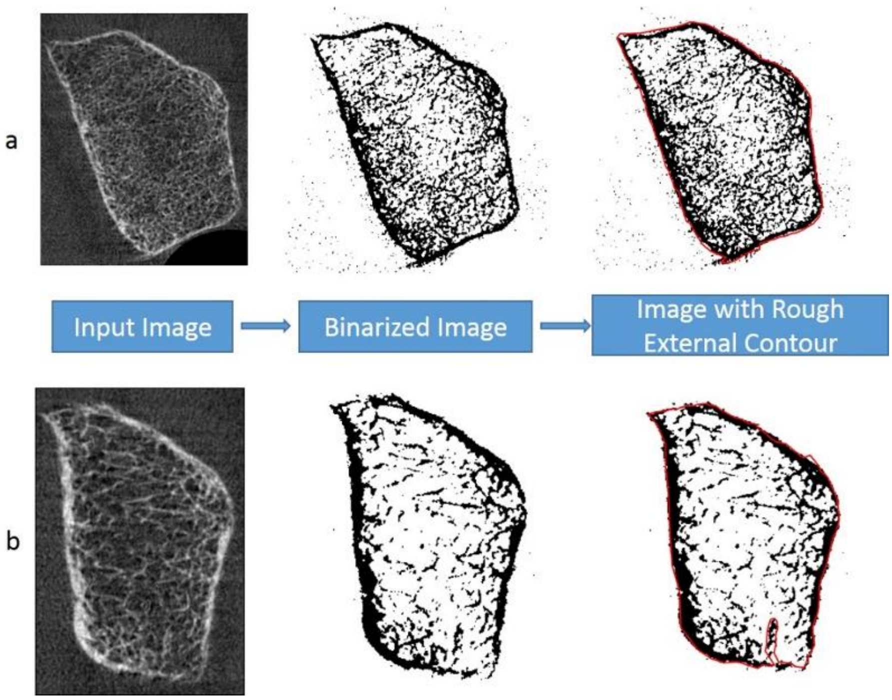


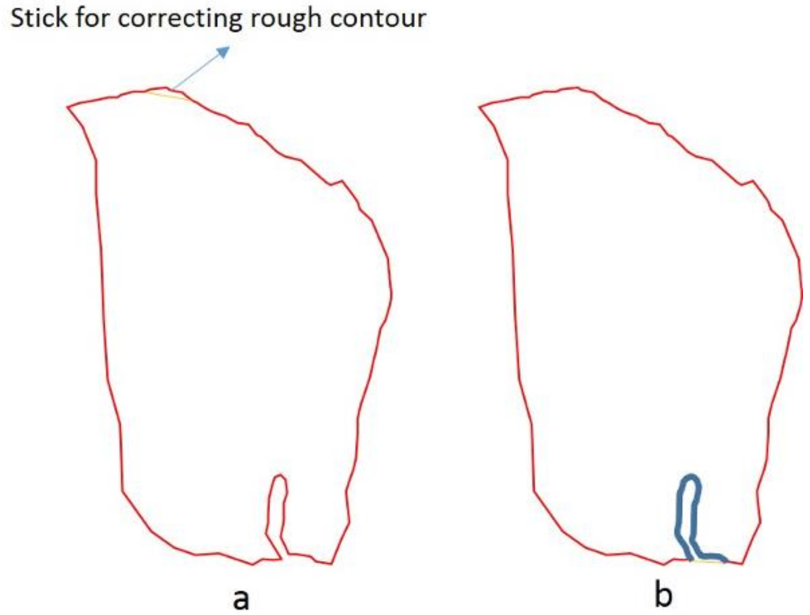
Fig. 6: Contour Process

The rough external contour detection in (a), an example of "good" rough contour is presented; in (b), the rough contour is "bad" as the very thin cortex.

In some cases where the bones with very thin cortex, we need to correct the rough external contour. The outer layer of the bone should be cortex and the rough external contour shall be the voxels along this outer layer, as shown in figure above (a). In some images, however, the outer layer is not closed because of the very thin cortex, as shown in figure above (b). To correct the contour, we originally raised an algorithm.

With the knowledge that shape of radius bone on a cross-section slice is locally convex, the correction algorithm is proposed as following:

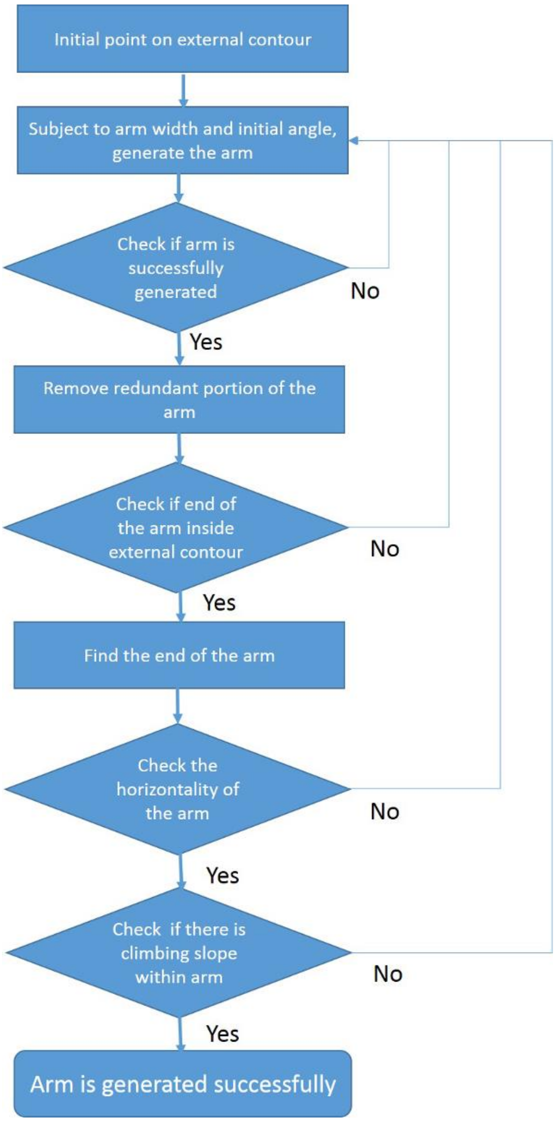
1. As shown in figure below (a), a 'stick' moves along the rough external contour voxel by voxel to correct the contour. Because the radius bone is locally convex, the length of the 'stick' shall be small enough. We choose the length of the 'stick' as the width of the arm. We will explain the arm in the next section



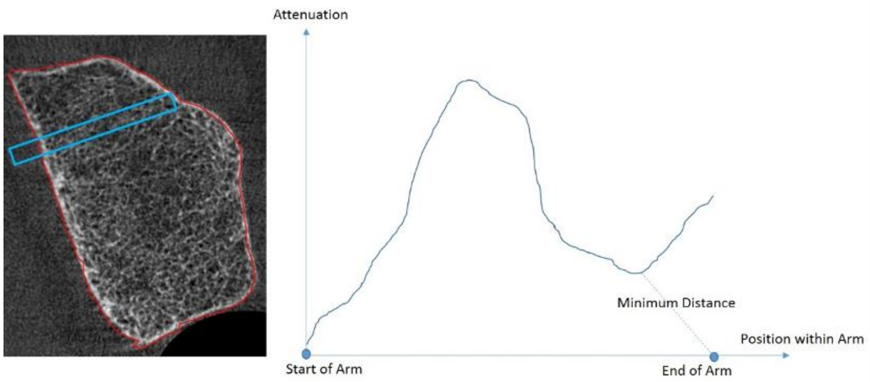
2. As shown in figure above (b), the "stick" (yellow) divides the contour into two parts: red and blue. Then, the ''stick" and red contour form into a new contour. Subsequently, checking the geometrical relationship between the blue contour and the new contour (red plus yellow). If the blue is inside the new contour, replacing the original contour (red plus blue) with the new contour; otherwise, move the "stick" forward by one voxel.
3. Repeating step 1 and step 2 until the contour cannot be updated.

6.3.1.5. Arm Analysis

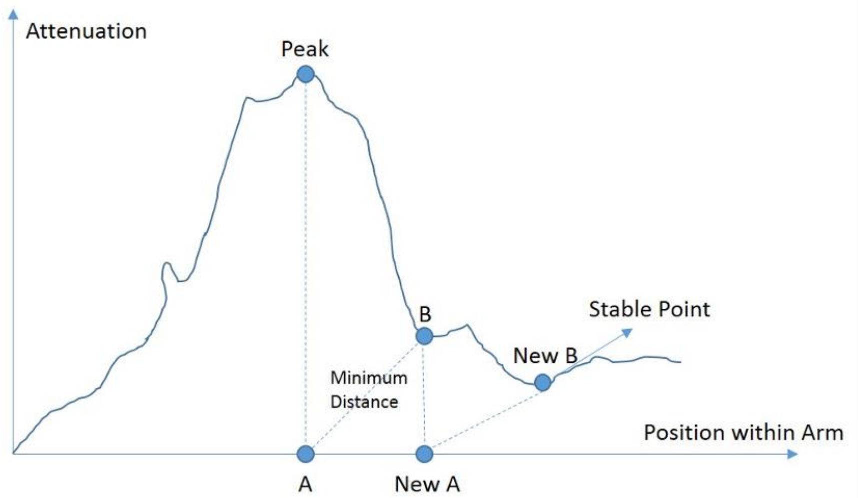
After identifying the external contour, the arm will be generated and analysed along it. As explained above, an arm is rectangular region of interest. To generate a proper arm, the width, direction, and position need to be decided. By referring to figure below, the algorithm of arm generation is illustrated.



- Identifying an initial point on the contour to create the arm. Subject to the arm width and initial angle, the arm is created. The arm shall have the ability to capture the pores of the cortical bone. The width of it cannot be too big or too small. We assign the width of arm as 3 times of the pore size (900 micron). Initially, the arm is created perpendicular to the tangent of the external contour.
- Removing the redundant part of the arm. After arm is created, the attenuation profile will be analysed, as shown in figure below. Arm will classify the voxels in the ROI close to the external contour. Therefore, the arm portion close to the opposite side of the external contour shall be considered as redundant. It is identified as the portion between the arm end and the point, from which the minimum distance is found from "right-bottom" corner of the attenuation profile.

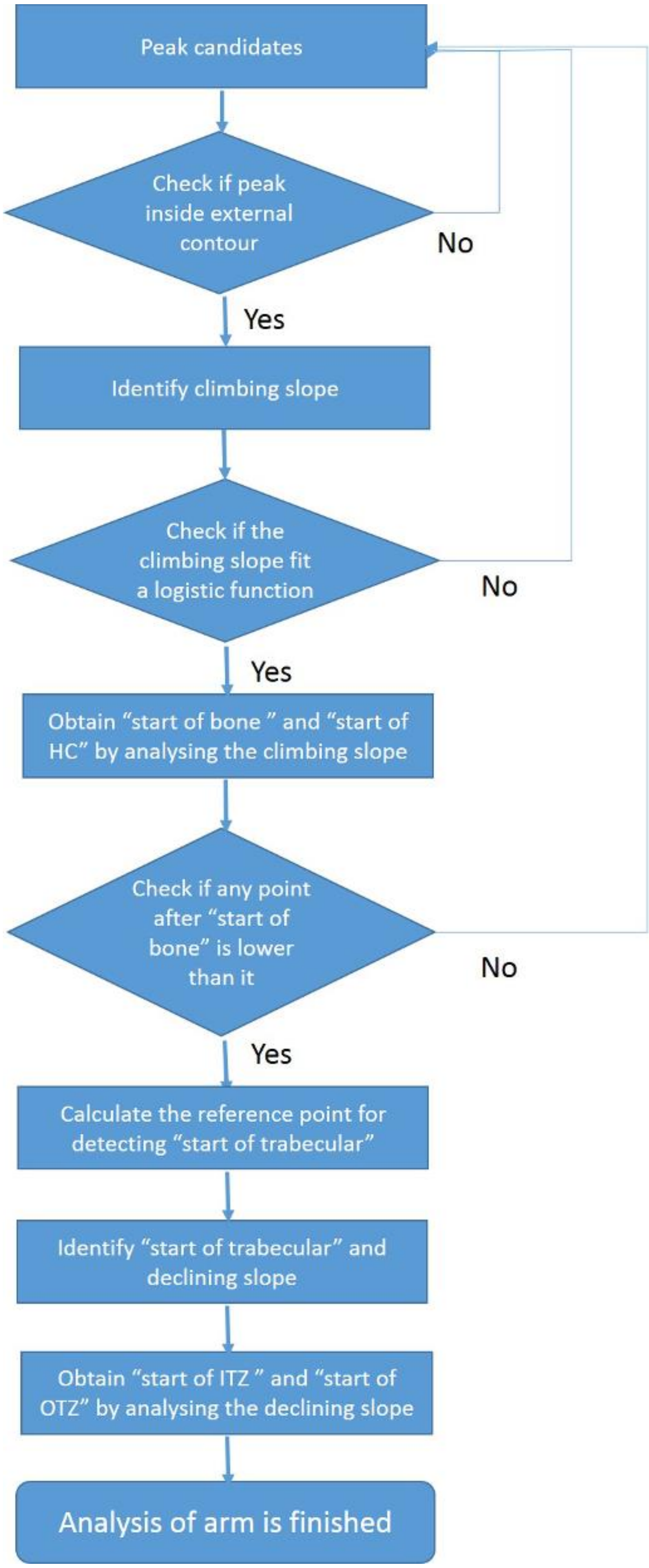


- After removing the redundant portion of the arm, the arm will be checked against the external contour. If the end of arm is outside the contour, back to step 1, change the angle and create a new arm; otherwise, it goes to next step.

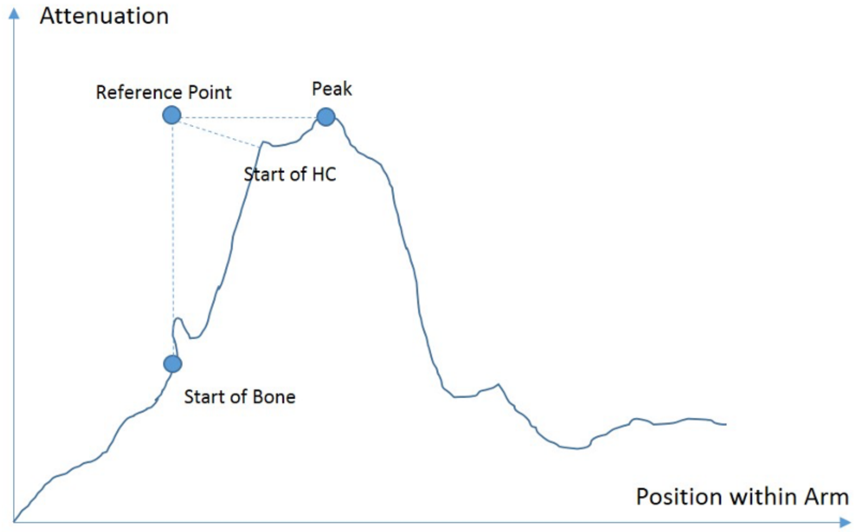


- In order to ensure the arm doesn't contain too many redundant voxels, the end of the arm will be re-defined. To do this, the point with maximum attenuation value on the profile will be detected. From this point, the third "stable point" on the x axis towards the end of arm shall be identified and assigned as the new end of the arm. As shown in the figure above, from point A on x axis, towards end of the arm, the point B on the curve with minimum distance is found. If point B is with the same x value as point A, point B is considered as a stable point of A; otherwise, point A1 is created by taking the x value of point B, point B1 shall be found.
- After the new arm is determined, the "horizontality" of the arm needs to be checked. Ideally, the bone matrix included in the arm region should be homogenous. To check this, the average value of rows in the arm are first regressed into a linear line function. We then use the slope of the line function to indicate the horizontality of the arm. If the "horizontality" of the arm is not accepted, back to step 1, change the angle and create a new arm; otherwise, it goes to the next step
- Checking if there is "climbing" slope between the start of arm and the maximum point detected in step 4. If not, go back to step 1, change the angle and create a new arm; otherwise, the arm has been generated successfully. Once arm is successfully generated, the

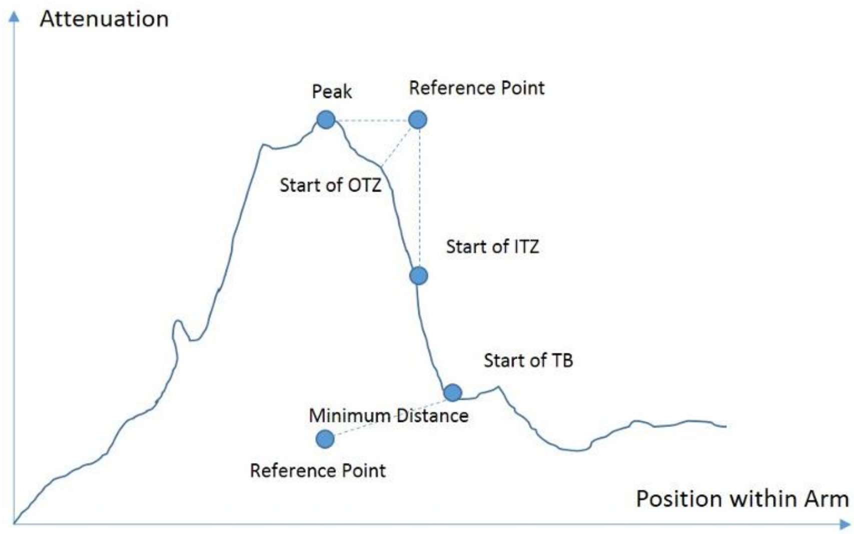
analysis of the arm starts. The algorithm of the arm analysis is presented in figure below.



- Identifying and sorting the peak candidates on the attenuation profile of arm. The first candidate the point with maximum attenuation on the profile
- Check if the peak candidate inside the external contour. If not, go back to step 1 and try the next peak candidate; otherwise, it goes to the next step.
- Detecting the point with the minimum distance towards the start of arm from the peak point (step2). Identifying the arm portion between the peak point (step2) and the "minimum distance" point as climbing slope
- Check if the climbing slope fits a logistic function. If not, back to step 1 and try the next peak candidate; otherwise, it goes to the next step
- As shown in figure below, identifying the "start of bone" as the point with the biggest change ratio on the longest climbing curve of the climbing slope. Create a reference point by taking the attenuation value of "peak" point and the x value of "start of bone" point. From this reference point, the point with minimum distance between "peak" point and "start of bone" point shall be detected "start of hard cortex" point.



- Check if there is any point after "start of bone" point with a lower attenuation. If not, back to step 1 and try the next peak candidate; otherwise, it goes to the next step.
- The median attenuation between the "minimum distance" point (step3) and the end of arm is calculated. A new reference point is created with the y value of the median attenuation and the x value of peak point. The "start of trabecular compartment" point is detected as the point with minimum distance from the new reference point towards the end of arm. Identifying the arm portion between the peak point (step2) and the "start of trabecular compartment" point as declining slope.



- As shown in figure above, identifying the start of inner transitional zone as the point with the biggest change ratio on the longest declining curve of the declining slope. Create a reference point by taking the attenuation value of "peak" point and the x value of "start of inner transitional zone" point. From this reference point, the point with minimum distance between "peak" point and "start of inner transitional zone" point shall be detected "start of outer transitional" point.
- After identifying all the key points, voxels within the arm will be classified into different compartment: background, hard cortex, outer transitional zone, inner transitional zone, and trabecular compartment.

6.3.1.6. Refinement

In order to minimise the segmentation error, refinement is designed. There are two steps for refinement: external contour refinement and internal structure refinement. Due to the limited resolution of the imaging system, partial volume effect occurs in adjacent regions between soft tissue and bone. After the arm rotation and analysis, most voxels effected by the partial volume loss will be eliminated. To optimise it, we check the densities of voxels along the external contour against the density of background (soft tissue). The voxel will be classified as background if its density is inferior to the density of soft tissue.

With the knowledge that bone compartments are separated, we refine the internal structure of the bone. We refine compartment by compartment. For each compartment, we connected the voxels into blobs. We keep the largest blob. To refine the other blobs, we classify them as the compartment which has appeared the maximum number of times in the surrounding voxels.

6.3.2. Index Calculation

After segmentation, the entire bone has been classified into four compartments: hard cortex, outer transitional zone, inner transitional zone, and trabecular compartment. Based the bone structure segmentation, StrAx Porosity Score (SPS) and StrAx Trabecular Score (STS) are calculated to assess the cortical bone and trabecular region. Structural Fragility Score (SFS) is then calculated based on SPS and STS. SFS captures the concurrent deterioration of cortical and trabecular bone.

6.3.2.1. StrAx Porosity Score (SPS)

SPS is the porosity of the cortical compartment defined as hard cortex plus outer transitional zone. As explained in our method paper [4], quantification of porosity in vivo is challenging because the median size of Harversian canal is around 50 micron. A significant proportion of voxels overlying cortical bone are composed of varying proportions of void volume and mineralised bone matrix volume. Thus, porosity is quantified voxel by voxel. The proportion of voxel volume occupied by mineralised bone matrix volume is its level of fullness (LOF). LOF is estimated by knowing the attenuation of a voxel that contains no mineralised bone and the attenuation of a voxel that contains only mineralised bone. Therefore, the LOF of voxel [*i*] is calculated as

$$LOF_i = \frac{I_i - P}{B - P} \quad (2)$$

where I_i is the attenuation of voxel i , P is the background attenuation, and B is the attenuation produced by a voxel containing only fully mineralised bone.

The void content or level of emptiness (LOE) of each voxel is

$$LOE_i = 1 - LOF_i \quad (3)$$

SPS is the average of all LOE of all voxels of the cortical compartment plus outer transitional zone. It is calculated as

$$SPS = \sum_{i=1}^{i=n} LOE_i \Big/ n \quad (4)$$

where n is the total number of voxels within the cortical compartment plus outer transitional zone.

6.3.2.2. StrAx Trabecular Score (STS)

STS is the average density D_T of voxels within the marrow cavity. The marrow is defined as the trabecular compartment excluding the transitional zone. It is calculated as:

$$D_T = \sum_{i=1}^{i=n} D_i \Big/ n \quad (7)$$

where n is the total number of voxels within the trabecular compartment.

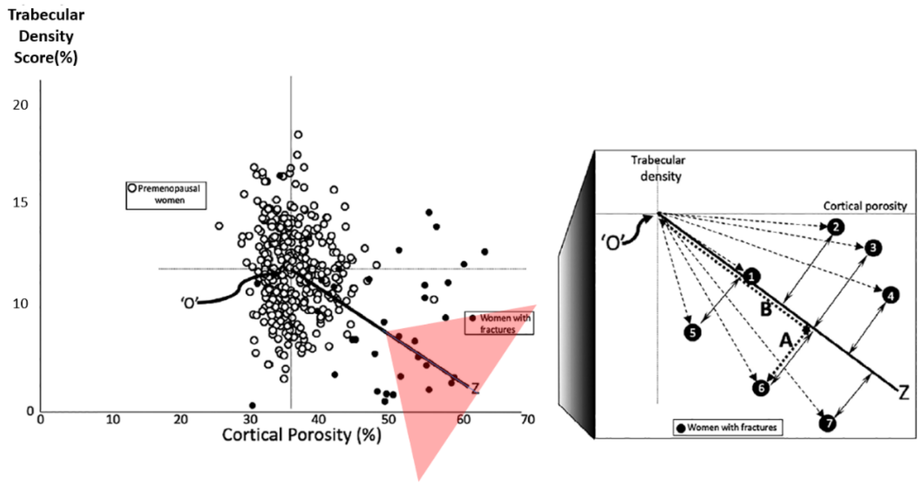
In order to express STS as a percent, D_T is normalized as:

$$STS = (D_T - D_{min}) \Big/ (D_{max} - D_{min}) \quad (8)$$

where D_{min} is minimum density, and D_{max} is the maximum density.

6.3.2.3. Structural Fragility Score (SFS)

We hypothesized that a surrogate measure of bone fragility will capture both the absolute and relative deterioration in cortical and trabecular bone produced by age- and menopause- related bone loss. Demonstration of deterioration in both cortical and trabecular bone is needed because bone loss affects both traits. A deficit in only one trait is likely to reflect errors in positioning of the region of interest, not microstructural deterioration.



The figure above is simplified to explain the derivation of the SFS more clearly. O is the mean of cortical porosity and trabecular density in 324 healthy premenopausal women. The slope of the regression line was derived using regression analysis of these traits in 33 postmenopausal women with fractures. A woman's (x, y) values are projected onto the regression line to quantify the absolute and relative deterioration in these two traits. For women with (x , y) coordinates on the regression line, distance B is the absolute deterioration in cortical and trabecular bone. The further the (x , y) coordinates are from O along the regression line, the greater the absolute deterioration in both traits and the greater the distance B. The perpendicular distance A captures the differing relative deficits. Women with coordinates above the regression line have relatively more severe cortical than trabecular deterioration. Women with (x , y) values below the regression line have the opposite. The SFS = B – A. For women with (x , y) coordinates on the regression line, A is zero. When distance A is large, the greater the likelihood that there is a deficit in only one trait, suggesting the deficit is the result of an error in positioning the region of interest, not bone loss.

The area of the red cone in the figure above indicates a high-risk area where SFS = B - A is greater than or equal to 70. For patients 2, 3, and 4, the deterioration in cortical porosity is greater relative to deterioration in trabecular density. For patients 5, 6, and 7, the deterioration in trabecular density is greater relative to the deterioration in cortical porosity. The SFS captures these varying absolute and relative deteriorations in cortical porosity and trabecular density.

SFS is an index score. The index assesses fracture risk through the concurrent measurement of deterioration of both cortical and trabecular bone. The predictive strength of SFS is supported by clinical studies. The following table is a cohort summary of the clinical studies.

Clinical Trial	**Cohort**	**Geographic Location**	**Gender**	**Age, mean (SD)**	**Ethnicity**
Mayo Study, cross-sectional design, SFS vs TBS fracture diagnostic	204 postmenopausal women	United States	Female	66 years old (9 years)	Caucasian
OFELY study, prospective design, SFS vs TBS predicts fracture	589 postmenopausal women	France	Female	68 years old (9 years)	Caucasian
Treatment follow-up study, SFS in monitoring effects of treatment	247 postmenopausal women	United States, Argentina, Canada, France, Australia	Female	60 years old (5 years)	Caucasian (96%), Hispanic (1%), Asian (3%)
SFS in monitoring bone deterioration through menopause	370 women (113 were post-menopausal, 45 were peri-menopausal, and 212 were pre-menopausal)	Australia	Female	48 years old (5 years)	Caucasian
Head-to-head study, SFS measured with Strax HR-pQCT vs Scanco HR-pQCT	54 women, of them were fracture free and 29 of them had fracture history	Australia	Female	64 years old (7 years)	Caucasian