

ENGLISH



Instructions for Use

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Este es un software médico para uso exclusivo en clínicas.



1.1.0



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1. INTRODUCTION

1.1. Intended use

Online Ultrasound Image Segmentation System (OSIS) Ovary is a web-based online platform, using Artificial Intelligence (Deep Learning), with the purpose of providing objective anatomical measurements of the different ovarian follicles (folliculometry) from a three-dimensional (3D) transvaginal ultrasound. The software runs on a centralised server and its results can be accessed via a standard computer browser. OSIS Ovary can be used to perform automatic segmentation of the ovarian follicles, 3D representation of the segmentation and quantification of each of the follicles detected, providing quantitative measurements of the follicles. This device is indicated for monitoring the treatment of adult women, mainly women undergoing controlled ovarian hyperstimulation (COH) cycles. Not indicated for paediatric use.

1.2. Intended user

OSIS Ovary is intended for use by healthcare professionals in the area of assisted reproduction, i.e., only by personnel assigned to the patient (gynaecologists, nurses) qualified in the use of 3D gynaecological ultrasound with transvaginal probe.

Not intended for home use or non-professional users.

1.3. Medical condition

Controlled monitoring of ovarian hyperstimulation and estimation of when follicles are mature for follicular puncture is carried out by means of hormonal analysis and periodic transvaginal ultrasound scans in which the number of mature follicles and their sizes can be seen in order to predict the date of ovarian puncture when there are several (3 or more) follicles that reach a certain size (usually greater than 16-17 mm) in mean diameter (folliculometry).

This is an arduous task that requires a specialist doctor (gynaecologist) devoting a great deal of time to manual measurement directly on the transvaginal ultrasound, in addition to the subjectivity and errors involved. Furthermore, it must be taken into account that in each session both ovaries are analysed and that during each hyperstimulation treatment between 3 and 6 ultrasound scans are performed per patient, meaning a high number of ultrasound scans per day.

OSIS Ovary is indicated for the treatment and monitoring of adult women, mainly women undergoing controlled ovarian hyperstimulation cycles (also called COH), as a tool for folliculometry (providing objective anatomical measurements of the different ovarian follicles) from any three-dimensional (3D) transvaginal ultrasound system, during the cycle, from the beginning until the collection of oocytes to be fertilised in vitro. Not indicated for paediatric use. OSIS Ovary provides the number and size of follicles at different patient visits.

Often, even if mature follicles are harvested, they do not contain an oocyte inside. In this case the whole process needs to be repeated with the patient from the beginning. In the event OSIS Ovary gives an error, the doctor could avoid it by manually measuring it on the ultrasound and basing their decision on their experience and other clinical values external to OSIS Ovary to provide the correct guidelines for the following steps of the process. In the worst case, no harm could be done to the patient other than lengthening the time to get pregnant and repeating the same process from the beginning.

1.4. Clinical benefits

The clinical benefits of this software as a medical device are indirect. In other words, the device itself does not directly have a positive impact on patients, but it allows a procedure to be performed. The indirect clinical benefits of OSIS Ovary are as follows:

- OSIS Ovary improves the patient's quality of life as it improves the practitioner's clinical management of the patient by providing objective and accurate quantitative measurements of the patient's follicles and streamlining the treatment process.
- It objectively quantifies the number and size (relaxed diameter or d(V) and volume) of follicles, with the precision of a gynaecologist, present in women's ovaries throughout the controlled ovarian hyperstimulation (COH) cycle. These measurements are used in current clinical practice during the cycle to adjust, along with the patient's other clinical information, the treatment administered to the woman and to schedule folliculometry.
- OSIS Ovary performs the intended function (implying that there is a clinical benefit in doing so).

In summary, the clinical benefits of OSIS Ovary are the positive impact related to its function to facilitate and expedite the practitioner's management of the patient from 3D transvaginal ultrasound in the folliculometry process to continue with the process.

1.5. Target patient population

Adult women, mainly women undergoing controlled ovarian hyperstimulation (COH) cycles.

1.6. Technical product claims

OSIS Ovary is a stand-alone medical software product for:

- Enabling automatic segmentation of ovarian follicles present in 3D transvaginal ultrasound scans of women using an Artificial Intelligence (AI) algorithm.
- Allowing visualisation of segmentation in 2D and 3D.
- Objectively quantifying the number and size (relaxed diameter or d(V) and volume) of follicles, with the precision of a gynaecologist, present in women's ovaries throughout the controlled ovarian hyperstimulation (COH) cycle.
- Allowing the professional to perform quality control to validate the results or to discard incorrect results once they have been reviewed, as well as the correction of the measurements provided, after manual measurement with a ruler in the different 2D planes as is now the case in current clinical practice.

1.7. Indications

- This device is indicated for monitoring in the treatment of adult women, mainly women undergoing controlled ovarian hyperstimulation (COH) cycles, as a tool for folliculometry during the cycle, from the start until the collection of oocytes.
- It is indicated for patients who have acquired 3D transvaginal ultrasound images that include the entire region of both ovaries.
- OSIS Ovary must be used with a 3D transvaginal ultrasound acquired with a GE scanner. Images must follow the image quality criteria provided in these instructions for use for correct output of OSIS Ovary.

1.8. Contraindications

- The device is contraindicated for any other medical use not indicated in the intended use of the device.
- Not for use in paediatric patients.
- Not for use in 3D transvaginal ultrasound taken with a non-GE scanner.
- Not for use in 2D ultrasound imaging.

After extensive pre-clinical research into possible contraindications to the use of the device, no known contraindications to OSIS Ovary were identified, as well as no undesirable side effects from its use.

1.9. Residual risks

After performing the risk management of OSIS Ovary in accordance with the ISO 14971: 2019 standard, ISO/TR 24971:2020 and the medical devices regulation, MDR 2017/745, it is concluded that all the risks of OSIS Ovary are reduced as far as possible and all of them are acceptable and therefore, the medical device does not present residual risks that must be communicated to the user in the IFUs.

1.10. Any undesirable side effects

OSIS Ovary does not have any undesirable side effects.

1.11. About these instructions for use

- Please read and understand these instructions for use provided with the software before attempting to use OSIS Ovary.
- Please check that the version of the instructions for use matches the version of OSIS Ovary you wish to use.
- The instructions for use are available in the Help option of the OSIS Ovary platform, as well as on the OSIS Ovary About tab page. Instructions for use are also available on the Fertoolity website: <https://fertoolity.com/es/manuales-usuario>.
- The instructions for use are only available in PDF. They can be consulted using the free reader available at: <https://get.adobe.com/uk/reader/>.
- These instructions for use are only provided in electronic format. If you need them in paper format, please contact the Fertoolity team at info@fertoolity.com and request the instructions in hard copy. To do so, you will need to provide a Full Name associated with an OSIS Ovary user, a telephone number, an email address and a physical address where you would like to receive the paper instructions for use. The user will receive the paper instructions for use, at no additional cost, within 7 working days of receipt of the request.
- It is recommended that the user keeps these instructions for use together with the product for future reference.
- The images in these operating instructions are to help the user's understanding only. In some cases, they may differ slightly from what you see on the screen.
- All references to norms, regulations, standards and their revisions are valid at the time of publication of these operating instructions.

1.12. Declaration of Conformity

This product conforms to the following norms, regulations and standards:

- MDR 2017/745: Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices.
- EN ISO 13485:2016+A11:2021 - Medical devices. Quality management systems. Requirements for regulatory purposes
- EN 62304:2006+A1:2015 - Medical devices software - Software lifecycle processes
- EN 82304-1:2017 - Healthcare software. Part 1: General requirements for product safety.
- EN 62366-1:2015+AC:2015+AC:2016+AC:2016+A1:2020 - Medical devices - Application of usability engineering to medical devices
- EN ISO 14971:2019+A11:2021 - Medical devices - Application of risk management to medical devices - Risk management application to medical devices
- ISO/TR 24971:2020 - Medical devices. Guidance on the application of ISO 14971.

- EN ISO 15223-1:2021 - Medical devices. Symbols to be used with information to be supplied by the manufacturer. Part 1: General requirements
- EN ISO 20417:2021 - Medical devices. Information supplied by the manufacturer.
- IEC/TR 80002-1 Medical device software - Part 1: Guidance on the application of ISO 14971 to medical device software
- ISO/IEC/IEEE 12207:2017 Systems and software engineering. Software life cycle processes.

1.13. Security Notes

- The OSIS Ovary platform is a diagnostic and treatment monitoring tool. It in no way presents, predicts, suggests or forecasts the patient's diagnosis.
- The final diagnosis of the study is the sole responsibility of the professional, so the results provided by the platform must be verified before finalising the analysis of the cases. A case should not be automatically closed or concluded without first checking that the results provided by the platform are correct. The software is intended to assist the clinician and cannot completely replace their clinical judgement.
- Do not include personal patient information during data export from the ultrasound machine that could compromise the patient's identity.
- Before exporting images to OSIS Ovary from your ultrasound machine, make sure that these images correspond to the patient whose identifier you have entered in the ultrasound machine.
- The images to be exported must be 3D volumes of the ovaries of a patient who meets the requirements for use.
- Do not attempt to export screenshots or video from your ultrasound machine.
- The browser supported by the platform is Google Chrome version 100.0.4896.127 (and later).
- For the correct representation of the results in OSIS Ovary, a screen of at least 14 inches with a minimum resolution of 1920 x 1080 pixels is required.
- OSIS Ovary is not a real-time service. Images exported from your ultrasound machine will be queued for processing on the server. Please note that the delay you experience when exporting images will depend on the internet speed at your centre.
- In order for the platform to function correctly, the user is recommended to use a computer with the following minimum characteristics:
 - i3 processor or similar
 - 4GB RAM
- OSIS Ovary should only be used in combination with equipment that meets the defined and detailed minimum system requirements.
- The correct functioning of all the features of the platform when used from a mobile device (smartphone, tablet, etc.) is not guaranteed. It is always recommended to use the platform from a computer with the aforementioned features.
- The user should always verify that the information in the reports generated by the platform matches the corresponding case information displayed on the platform.
- The platform is intended exclusively for clinical use by professionals (doctors, nurses or technicians) experienced in the use of 3D gynaecological ultrasound with transvaginal probe.
- The use of OSIS Ovary requires specific training in the use of ultrasound equipment.
- Pay close attention when using OSIS Ovary, especially when interpreting the results. Any distraction may cause a misinterpretation of OSIS Ovary results and lead to a wrong decision about possible diagnoses, treatment follow-up or interpretations.
- Images obtained with transvaginal ultrasound equipment must be of adequate quality, i.e., contain the whole of the desired anatomy, show contrast in the different parts of the anatomy, and not be affected by high levels of noise or artefacts.
- OSIS Ovary does not guarantee the quality, accuracy or legality of the medical images (provided by the user) from which the software calculates the parameters. Therefore, the user should exercise caution when using the software.
- The final evaluation of the OSIS Ovary results should always be supervised by a physician

with expertise in the area of fertility.

- In the event of any eventuality, problem or query, the user should contact the Fertoolity Technical Service via email: info@fertoolity.com.
- The user should report any serious incident related to the product to Fertoolity (info@fertoolity.com) as well as to the competent health authority, in this case the AEMPS.

1.14. Symbols

Symbol	Meaning	Reference
	Manufacturer	EN ISO 15223-1 ISO 20417
	Date of manufacture	EN ISO 15223-1 ISO 20417
	See instructions for use	EN ISO 15223-1 ISO 20417
	Electronic instructions for use to indicate on the product or on its packaging that information relevant to the use of the product is available in electronic format instead of, or in addition to, printed on paper.	ISO 7000 - 3500
	Medical device	EN ISO 15223-1 ISO 20417
	Serial Number In the case of OSIS Ovary, the version of the software platform is provided.	EN ISO 15223-1 ISO 20417
	Unique Device Identifier or Unique Product Identifier	EN ISO 15223-1 ISO 20417
	The CE marking indicates compliance with the MDR 2017/745 medical device regulation in Europe. It is accompanied by the Notified Body number. The OSIS Ovary label shows XXXX as it does not yet have Notified Body approval. We are in the process of obtaining it.	MDR 2017/745

1.15. Nomenclature

- **2D:** 2 dimensions
- **3D:** 3 dimensions
- **AEMPS:** Spanish Agency for Medicines and Health Products.
- **HTTPS:** HyperText Transfer Protocol Secure
- **COH:** Controlled ovarian hyperstimulation.
- **AI:** Artificial Intelligence
- **AI:** Artificial Insemination
- **IVI RMA:** Instituto Valenciano de Infertilidad - Reproductive Medicine Associates

- **IP:** Internet Protocol
- **IVF:** In Vitro Fertilisation
- **LMP:** Last Menstrual Period
- **MDR:** Medical Device Regulation 2017/745
- **MDSW:** Medical Device Software
- **MRN:** Medical Record Number
- **OSIS:** Online System for Image Segmentation
- **OTS:** Off-the-shelf software
- **SIVIS:** IVI Information System
- **SOUP:** Software of Unknown Provenance
- **UDI:** Unique Device Identifier

1.16. OSIS Ovary Identification

- **BASIC UDI-ID:** 843702416165OSIS7J
- **UDI-DI:** (01)8437024165019
- **UDI-PI:** (21)V010100
- **GMDN:** 40873 → Ultrasound imaging system application software. An individual software program or a group of programs, routines or algorithms that add specific image processing and/or analysis capabilities to the configuration of an ultrasound diagnostic system. A basic set of application programs and routines are included with these computer imaging systems and may be upgraded to correct programming errors or to add new capabilities to the system. Some application software programs or program packages must be combined with specific hardware or firmware configurations to function as intended. Application software packages are usually identified by a unique name and a "version" or "update" number.
- **EMDN:** Z11049092 → Various ultrasound instruments – Software as medical device.
- **MDR CODE:** MDA 0315 Software.
- **PRODUCT CLASS:**
 - In accordance with MDR 2017/745, active medical device class IIa.
 - In accordance with EN 62304, Medical Device Software, class B.
 - In accordance with MDR 2002, Class I.

1.17. Information about the manufacturer



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2. GENERAL DESCRIPTION

OSIS Ovary is an online web platform for use in clinics specialised in reproductive medicine, which provides segmentation and objective anatomical measurements of the different ovarian follicles (folliculometry) based on the reception of ultrasound volumes (3D) of the ovaries, so that medical staff can use this information to control the monitoring of controlled ovarian stimulation (COS) of patients during in vitro fertilisation (IVF), oocyte vitrification or artificial insemination (AI) cycles, making folliculometry processes in clinics more flexible, as well as making clinical decisions.

Folliculometry is a procedure that involves periodic transvaginal ultrasound scans to monitor the growth of follicles in the ovary, measuring follicular size to monitor COH. It is a simple and routine procedure, performed 2-6 times during each ovarian stimulation cycle. Currently, manual folliculometry is performed by the gynaecologist in order to count the number of follicles per ovary and measure the diameter of the follicles, one by one (manual follicle measurement). This technique is considered the Gold-Standard in clinical practice.

OSIS Ovary enables the automation of ovarian follicle measurements (number and size), significantly reducing the hours spent by clinicians in processing and analysing these images, providing repeatable anatomical measurements of the different ovarian follicles in an objective way, and it can be used from any 3D ultrasound machine no matter where it is located.

The automatic segmentation of ovarian follicles is carried out using an Artificial Intelligence (Deep Learning) model. From this segmentation, OSIS Ovary calculates the number of follicles detected in an ovary and their average diameter.

OSIS Ovary is hosted at IVI RMA's central servers in Valencia in a dedicated facility under the supervision of the technical team and is designed to remotely receive (via the internal network between IVI clinics) Cartesian volumes captured with the 3D endocavity probes - usually for transvaginal use of General Electric Healthcare's Voluson Series ultrasound machines, via encrypted IP connection with Ethernet network cable. The OSIS Ovary platform can be accessed via the web browser of any standard "off-the-shelf" computer connected to the site's network and requires no installation on the user's computer. The user simply needs to have a username and password associated with a clinic and centre and be connected to the IVI RMA network.

When a new licence to use OSIS Ovary is created for a centre and a clinic, Fertoolity's IT team configures the platform to receive inputs from the 3D ultrasound machines in those clinics: the acquisition of the right and left ovary by a technician using a 3D transvaginal ultrasound machine (GE Voluson). All acquisitions made with those ultrasound machines that meet the criteria defined during setup will be sent to OSIS Ovary and analysed.

The user exports the volumes from the ultrasound machine to the OSIS Ovary server, which automatically processes the files received and performs follicle segmentation and quantification. Finally, users can access the OSIS Ovary web platform to view the reports, manually correct follicle quantification if necessary, and validate the report.

OSIS Ovary incorporates an alert logging system, which triggers alarm messages to the user when the ultrasound volume has not been correctly received, determining the specific cause detected and thus facilitating correction or resolution of the problem.

OSIS Ovary is equipped with a manual quality control system, which allows the medical staff to verify that the ultrasound volumes received are properly assessed, and to report and manually correct those that have not been processed correctly.

OSIS Ovary is designed to work with ultrasound Cartesian volumes saved (prior to export) on the local hard drives of General Electric Healthcare Voluson Series ultrasound machines. A copy of each volume exported to OSIS Ovary will also be stored on the OSIS Ovary server. This will enable subsequent remote reviews of the ultrasound data by the user or by Fertoolity Technical Support, if necessary.

2.1. Expected useful life

Hardware parts can rust, suffer wear, fatigue or any kind of ageing phenomena... However, in software nothing rusts or suffers wear. Performance degradations can be seen more as bugs than as ageing. E.g., if software slows down, it is because the memory or hard disk is full. This can be corrected by maintenance (emptying the hard disk) or bug fixes (fixing the memory leak).

The software's useful life will then depend on the context of use: when this context changes, the software becomes unusable.

Software as a healthcare product runs on hardware. When this hardware becomes obsolete, i.e., when the hardware manufacturer stops providing support, the software running on this hardware can no longer be used. In this case, obsolescence can be estimated based on the useful life of the

hardware generation. For example: the technical features of a current PC will still be found in a PC in five years' time.

The expected useful life that can be defined for software as a medical device depends on the technology used:

- software as a healthcare product running on a Windows PC could have a useful life of 3 to 5 years.

Software as a medical device needs SOUP/OTS to run. When the versions of the SOUP/OTS used by the software as a medical device become obsolete, Fertoolity can no longer maintain this software as a medical device. This is especially the case for security problems that are not fixed by the supplier of the SOUP/OTS. The software as a medical device can function with an obsolete version of a SOUP/OTS as long as there are no critical issues published in this SOUP/OTS. However, when that SOUP/OTS is an operating system or a browser, it is almost impossible to continue using the software as a medical device on a new major version of the operating system/browser, without revalidating the software as a medical device.

OSIS Ovary is a cloud software program and useful life is still a requirement for cloud software. Cloud software needs to be updated periodically to keep up to date with the continuous changes in the underlying cloud infrastructure. The software is only implemented in the cloud by Fertoolity's IT team and is therefore accessible to its customers. Customers are not required to install anything. This ensures that they always have access to the latest version of the software.

The only solution is to define a major release, a milestone in the cloud software lifecycle. All subsequent releases will be minor changes, until a new major version is released. The reliability of each release will follow the methodology described in the OSIS Ovary software development plan, which complies with the applicable technical standards: EN 62304, EN 82304, ISO/TR 80002 and ISO 14971.

Useful life and released versions are not the same. The useful life starts when a major version is released. After that, there may be several minor releases during the lifetime of the medical device software.

Defining a useful life compatible with medical device regulation requires monitoring SOUP/OTS, its updates and obsolescence, to assess whether changes in SOUP/OTS trigger major updates and revalidations of the software as a medical device.

Therefore, with all the above information, the defined useful life for OSIS Ovary according to the state of the art is 5 years, provided that the user follows the intended purpose of the product and the Instructions for Use provided. Before this time, a new major version of the software will be released and during this time the obsolescence of the SOUP/OTS (including the operating system and web browsers) and the obsolescence of the hardware will be monitored. If for these reasons a major version has to be released earlier (due to post-commercial information), this will be duly justified and the defined theoretical useful life of OSIS Ovary will be updated.

Sources:

- <https://www.johner-institute.com/articles/regulatory-affairs/and-more/what-constitutes-the-lifetime-of-a-medical-device-in-the-eu/#:~:text=The%20lifetime%20of%20a%20medical%20device%20is%20the%20period%20during,performance%20are%20no%20longer%20guaranteed.>
- https://www.johner-institut.de/blog/iec-62304-medizinische-software/lebensdauer-von-software/?__hstc=101363102.1d01e92c50a720bbf93cb200022919c0.1688916547636.1688916547636.1688916547636.1&__hssc=101363102.1.1688916547636&__hsfp=2272596688
- <https://blog.cm-dm.com/post/2022/02/25/Medical-Device-lifetime-and-SaMD>
- and Annex I MDR 2017/745, Chapter I GSPR No. 6

2.2. Duration of use

When talking about continuous use of a medical device, the concept of duration is considered, due to the fact that transient, short-term and long-term are defined in terms of continuous use. Continuous use should be understood as actual uninterrupted use for the intended purpose.

OSIS Ovary is software that will be used by the gynaecologist on a transient basis for each patient they check (less than 60 minutes) in continuous use. Therefore, we can consider the continuous use of the product to be transient. However, the gynaecologist uses the software in several follow-up sessions for the same patient during the whole ovarian stimulation cycle, until ovarian recovery occurs.

The information available in the software for a single patient could be consulted multiple times (by the gynaecologist) in the software in subsequent uses. As the software will be used for multiple patients, we can justify that it is a medical device for long-term use, even if its continuous use for the same patient in a single case of use is transient.

Therefore, the length of follow-up should be justified in terms of how long the efficacy of the treatment is expected to last and what it would take to demonstrate a positive benefit-risk conclusion compared to other SOTA treatment options.

We can consider the continued use of the product to be transitory. However, the practitioner uses the software in several follow-up sessions for the same patient during the patient's entire treatment process, which may take several sessions.

3. INSTALLATION

OSIS Ovary is distributed as a web platform and does not require installation by users on their computers. Likewise, uninstalling is not required. If you wish to stop using OSIS Ovary and have your data deleted, please contact the Fertoolity team by sending an email to info@fertoolity.com.

Both the server and the storage devices are deployed at the IVI RMA Group's dedicated facilities in Valencia. The user interface and the software required to process the ultrasound scans sent to OSIS Ovary from the ultrasound machines are installed on the server. This allows users (who are authorised) to access remotely at any time and from anywhere as long as they are using a computer with the minimum requirements within the IVI RMA Group network. This means patient data is kept anonymous and stored in a secure environment.

The Fertoolity team will take care of deploying OSIS Ovary at your centre so that all users will always have access to the latest version of the software, without having to worry about software updates.

The Fertoolity team will also take care of the maintenance of OSIS Ovary. The team will notify all users of each update by email with all changes and a link to the user manual.

In addition, as software as a medical device, there are no consumable or expendable items that must be used with the product.

3.1. Requirements

To be able to use OSIS Ovary, at least the following is required:

- A General Electric Healthcare Voluson Series ultrasound machine
- A PC with a screen size of at least 14 inches and a resolution of at least 1920 x 1080 pixels with an Intel i3 processor or higher and at least 4 GB of RAM.

- A browser and an Internet connection.
- All the aforementioned equipment must be connected and have authorised access to the IVI RMA Group network.

Once the medical staff has been registered by Fertoolity's Technical Service, they will receive an email notification to access the online web system. In this email the user will be provided with a link to select their secure password before accessing the platform. This ensures that no one else has access to each user's credentials at any time.

SIVIS users will be able to access the OSIS Ovary platform from within SIVIS without having to generate another password. However, they need to be authorised to access OSIS Ovary from the SIVIS portal by Fertoolity Technical Support.

Fertoolity's Technical Service will configure your clinic's ultrasound machine(s) to obtain correct connection and export of ultrasound volumes to the OSIS Ovary platform.

The Fertoolity team is not responsible for the regular maintenance of ultrasound machines, probes, computer equipment and network connections. Furthermore, to ensure a correct result of the ultrasound volumes processed in OSIS Ovary, the clinic staff authorised to perform ultrasound scans (doctors, nurses or imaging technicians) must be familiar with the technique of capturing and handling the export of ultrasound volumes, and may request additional training specifically for this purpose from Fertoolity.

3.2. How to start

To start using OSIS Ovary you will need the Fertoolity technical team to configure your ultrasound machines so that you can export volumes to the platform.

Likewise, the Fertoolity team will register a username with which you will be able to access the platform. To do this, you must provide the Fertoolity team with a valid email address to which a link will be sent so that you can enter a password before accessing the platform.

4. WORKFLOW

The workflow in OSIS Ovary starts with the export of a case from a configured ultrasound machine.

Once the machine is configured, the steps to export a case to OSIS Ovary are as follows:

Load the patient from the SIVIS appointment book in the same way as you do to send the ultrasound images. With the right mouse button select: 'Send to ultrasound machine' and select the ultrasound machine from which you will perform the scan. After a few seconds the data will be available in the ultrasound machine.

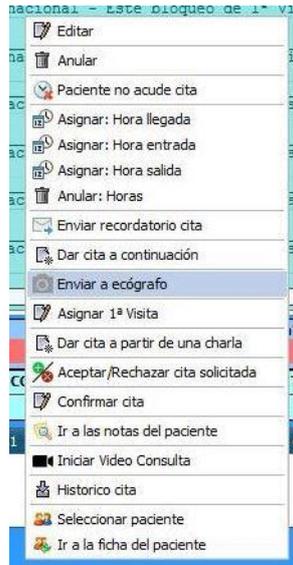


Figure 1. Appointment book options in SIVIS.

ID	AE Title	Clínica	Nombre
86	ECOVLC01	7 - IVI Valencia	ECOVLC01 [192.168.168.199]
87	ECOVLC02	7 - IVI Valencia	ECOVLC02 [192.168.168.198]
88	ECOVLC03	7 - IVI Valencia	ECOVLC03 [192.168.168.197]
89	ECOVLC04	7 - IVI Valencia	ECOVLC04 [192.168.168.196]
90	ECOVLC05	7 - IVI Valencia	ECOVLC05 [192.168.168.188]
91	ECOVLC06	7 - IVI Valencia	ECOVLC06 [192.168.168.194]
92	ECOVLC07	7 - IVI Valencia	ECOVLC07 [192.168.168.186]
93	ECOVLC08	7 - IVI Valencia	ECOVLC08 [192.168.168.192]
94	ECOVLC09	7 - IVI Valencia	ECOVLC09 [192.168.168.205]
95	ECOVLC10	7 - IVI Valencia	ECOVLC10 [192.168.168.189]
96	ECOVLC11	7 - IVI Valencia	ECOVLC11 [192.168.168.191]

Figure 2. Ultrasound worklist.

To select the patient, we have sent from SIVIS, press the button with the two people (Figure 3). Then select worklist (Figure 4).



Figure 3. Patient button.

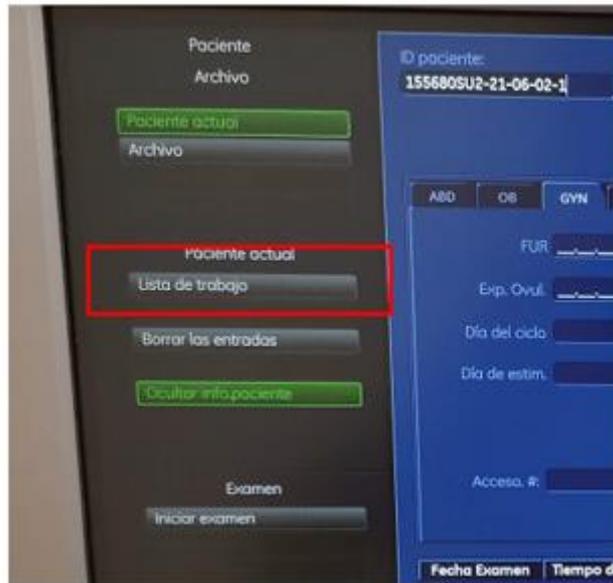


Figure 4. Worklist selection screen.

Select the patient and start the examination. We will see that the full name, date of birth and Medical Record Number (MRN) have been uploaded to the ultrasound machine.

Now we have to enter the **last menstrual period (LMP)** by hand. To do this, select the Gyn setting (Figure 5) on the left side menu shown in the Figure.

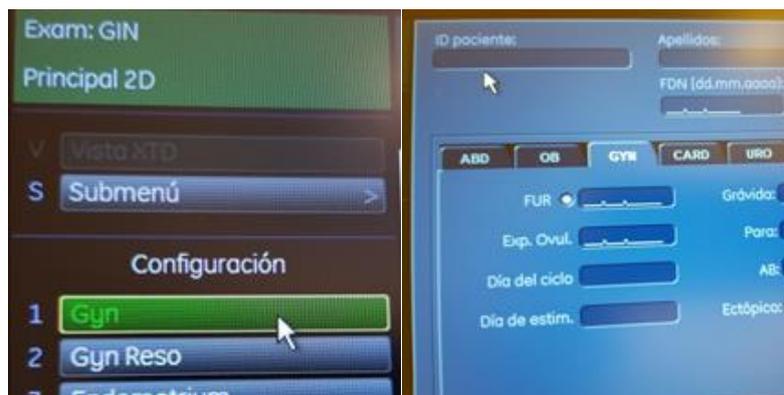


Figure 5. GYN menu to enter the LMP.

Next, proceed to capture the 3D volumes. **First the right ovary and then the left ovary.** To change ovary, use the lever provided for this purpose. Open the corresponding menu by pressing the 3D button. With the corresponding levers, select maximum quality and sufficient capture angle to ensure structures are not outside the volume. After scanning, save it as a **volume** with the **P1** button configured for this purpose.

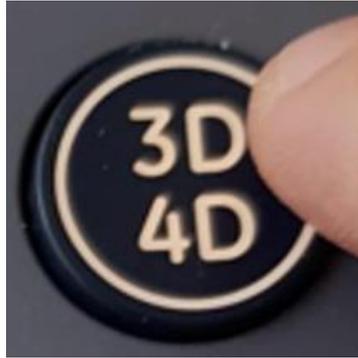


Figure 6. 3D volume capture button.



Figure 7. Ovary selection lever.

Finally, we will export the information. To do so, click on the **Archive** button.



Figure 8. File button.

Select the volumetric files of the two ovaries and choose the **Export option** on the left vertical menu.

Select **Unit NW2** in the case of the ovaries and **Unit NW3** in the case of the uterus.

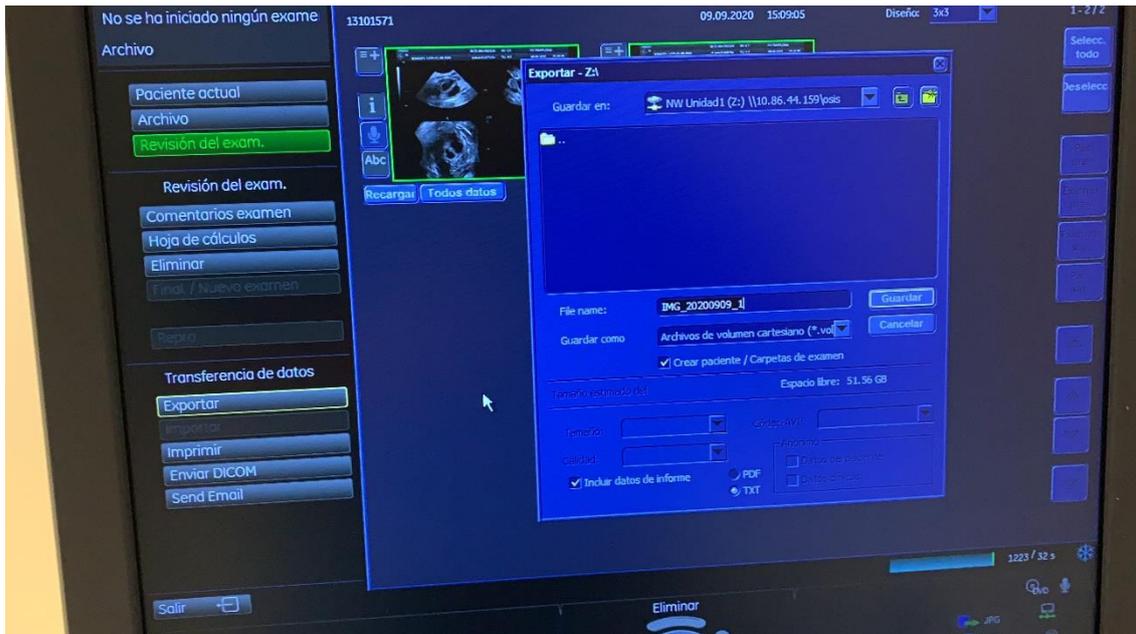


Figure 9. Export screen.

If the option '**create patient/exam folder**' is available, select it, click on **Save** and wait a few seconds until the export is complete.

Click on **Exit** to return to the starting point and continue with the next patient.

Once you have exported all the cases you need, you can log in to the platform with your username to review the results as described in sections 5 and 6 of this manual.

5. LOGIN

There are two ways for the user to access the OSIS Ovary platform:

- 1) Logging in from the Login screen (Figure 10, A): <http://osis.ivi.org>
- 2) Accessing from the SIVIS patient view by clicking on the OSIS link (Figure 10, B).

In both cases, your username must be registered on the platform. To register it, you can contact the person in charge at your centre or the Fertoolity team.

In this view it is possible to change the language (English, Spanish) before logging in as a user. After logging in, it will maintain the language selected by the user in the last session.

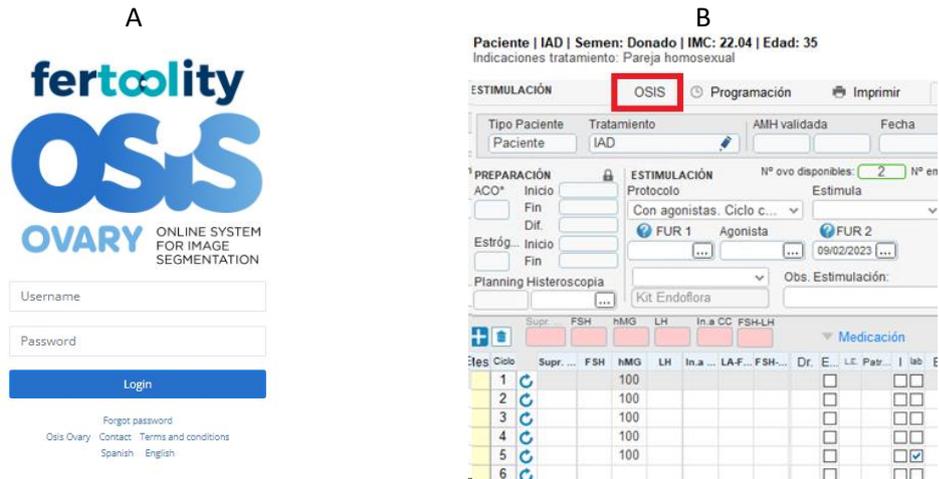


Figure 10. OSIS Ovary (A) and SIVIS (B) login screen.

6. ACTIONS YOU CAN TAKE WITH OSIS Ovary

6.1. Consult and/or accept the terms and conditions

You can access the terms and conditions before logging in by clicking on the "Terms and Conditions" link on the login screen (Figure 10).

Once you have logged in as a user, if you are a first-time user, the platform will direct you to the OSIS Ovary terms and conditions of use screen (Figures 11 and 12) where you must read and accept the terms and conditions in order to use the platform. You will not be able to use any of the platform's functions if you have not accepted the terms and conditions. In the event that these terms and conditions change, you will need to read and accept them again in order to use the platform.

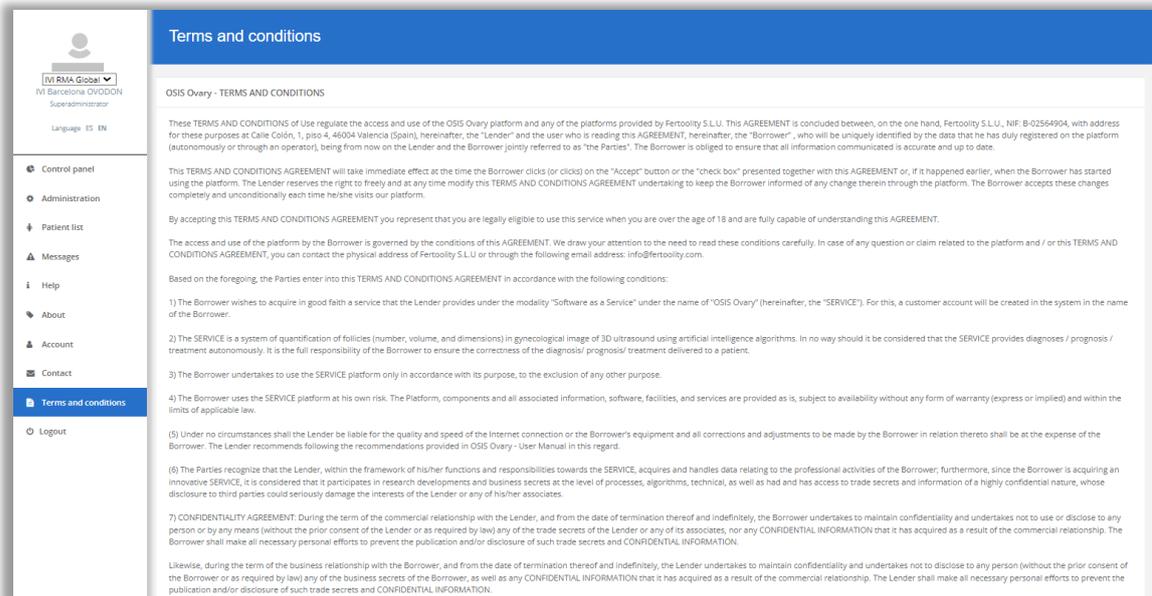


Figure 11. OSIS Ovary terms and conditions of use screen.

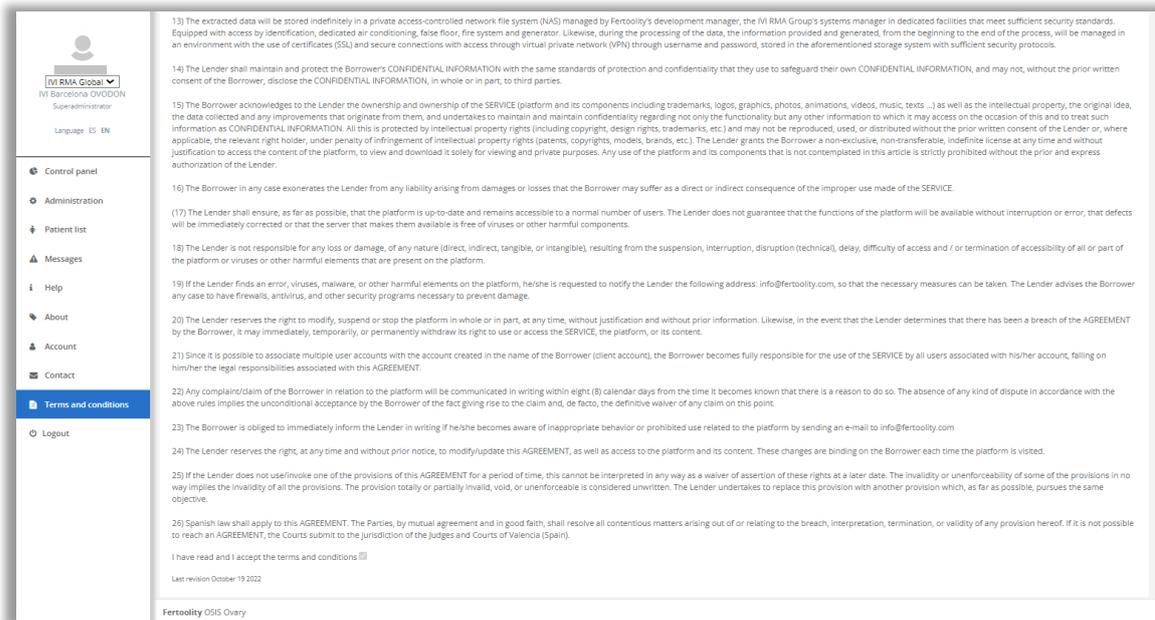


Figure 12. OSIS Ovary terms and conditions of use screen (acceptance box).

You can access the terms and conditions screen at any time by clicking on the side menu option (Figure 13) "Terms and Conditions". The terms and conditions are available in English and Spanish.

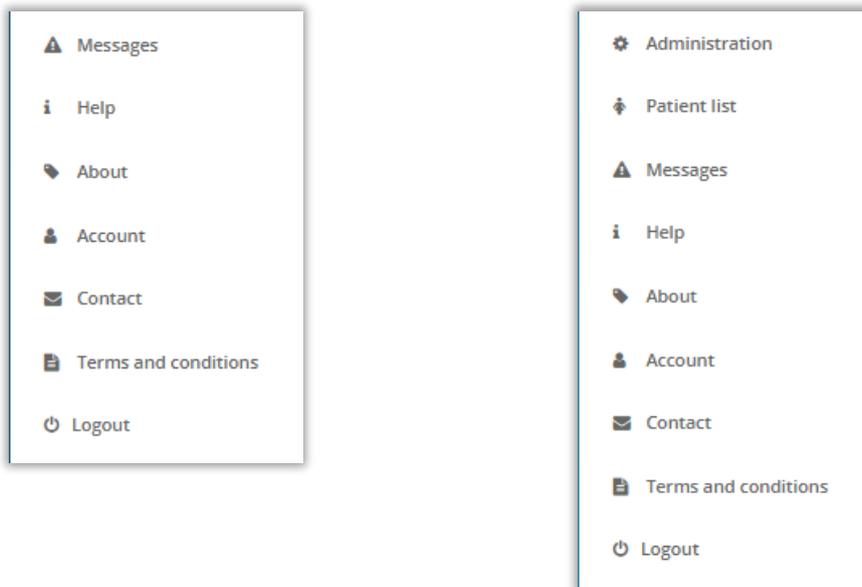


Figure 13. Side menu, on the left the basic user's menu, on the right the site manager's menu.

6.2. See product label

You can view the product label (Figure 14) before logging in as a user from the login screen (Figure 10) by clicking on the "OSIS Ovary" link.

The elements that appear on the label are detailed in the Symbols section (section 1.7).

In addition, you can find

- the UDI, which is a medical device traceability number and identifies this particular software with its UDI-DI (01), and UDI-PI (11) and (21).
- a link to the latest version of the OSIS Ovary user manual.

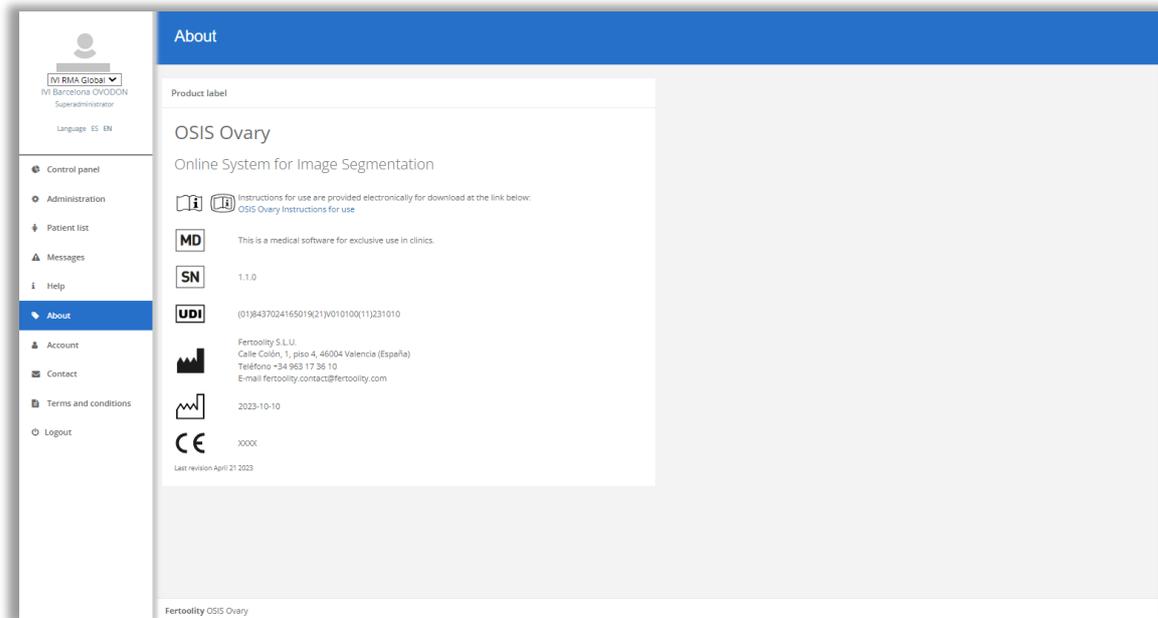


Figure 14. OSIS Ovary product label screen.

Once you are logged in as a user, you can access this screen by clicking on the side menu option (Figure 13) "About".

6.3. Contact the OSIS Ovary Team

You can contact the OSIS Ovary team by sending an email to info@fertooolity.com. You can easily access this email address by clicking on the "Contact" link on the login screen (Figure 10) or the "Contact" menu option on the side menu (Figure 13).

6.4. Download the user manual

You can download the user manual once you have logged in from the Help (Figure 15) or Product Label (Figure 14) screens which can be accessed from the side menu options (Figure 13) "Help" and "About" respectively.

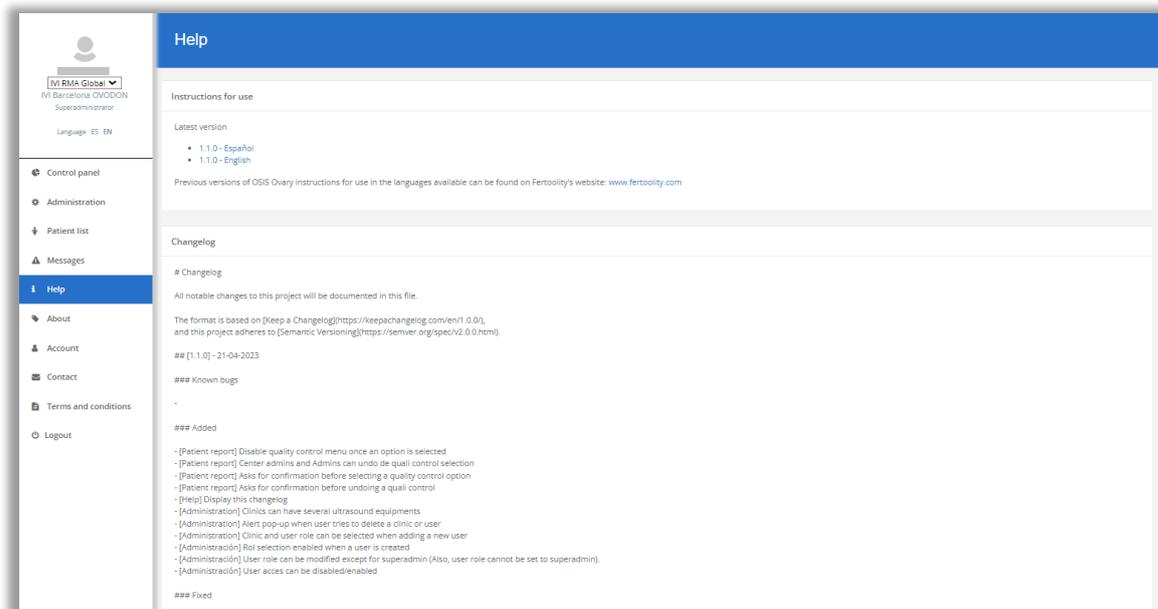


Figure 15. OSIS Ovary help screen.

6.5. Change your password and view account information

You can change your password from the Account screen (Figure 16), in the "Change password" section. You can access from the side menu option (Figure 13) "Account".

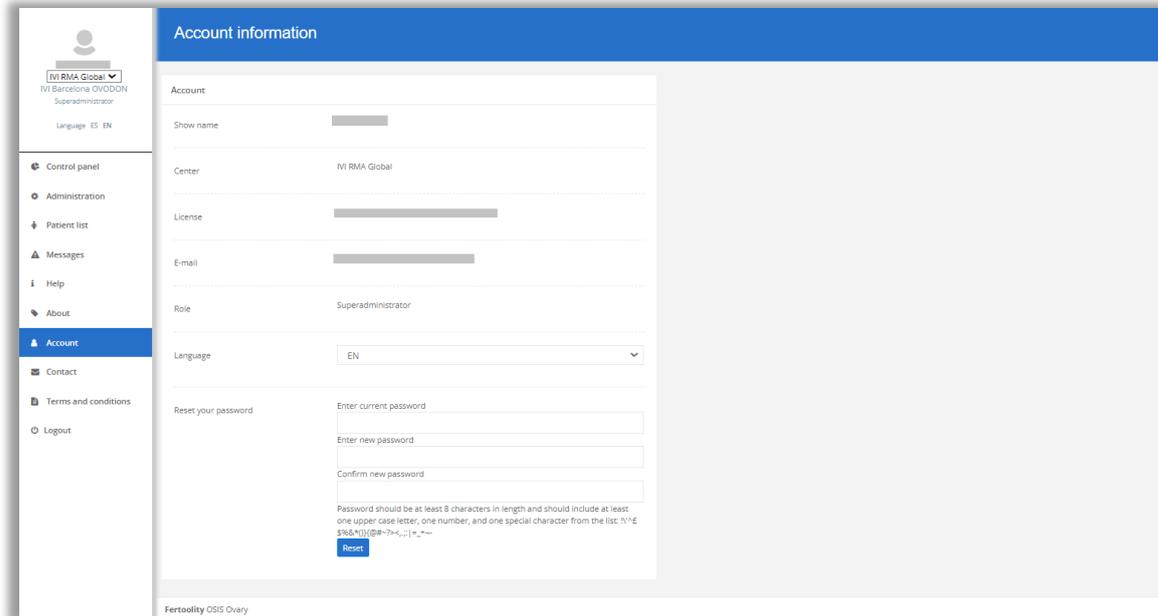


Figure 16. OSIS Ovary user account information screen.

In addition, on this screen, the user can consult the e-mail they are using to access the platform (E-mail), the centre where they are been registered (Centre), the licence through which they are accessing the service and its status (Licence), the level of privileges of their username (Role) and the current language selected and change it (Language).

6.6. Recover your password

If you have forgotten your password, you can set a new one by clicking on the "Forgot your password" link on the login screen (Figure 10). The platform will take you to a new screen to enter the email account you use to log in to the system (Figure 17).

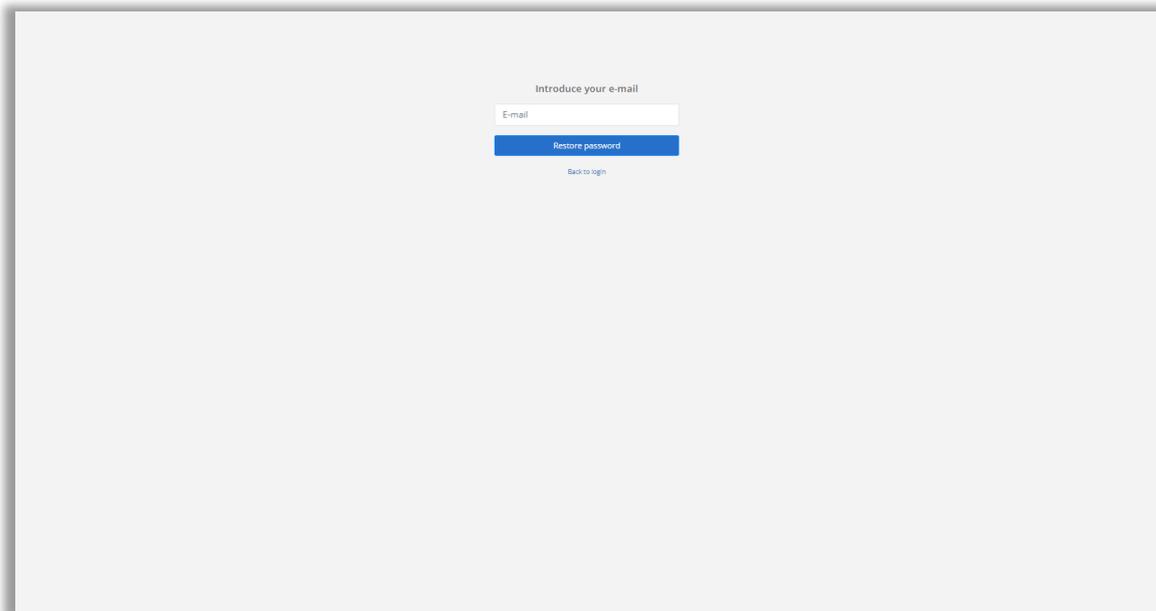


Figure 17. Screen to start the OSIS Ovary login password recovery process.

Enter your email address and click on the "Reset password" button. You will receive an e-mail with a link to access the screen where you can enter a new password (Figure 18). Please note that this link will only be valid for 15 minutes. After this time, you will have to re-request a password reset by clicking on "Forgot your password".

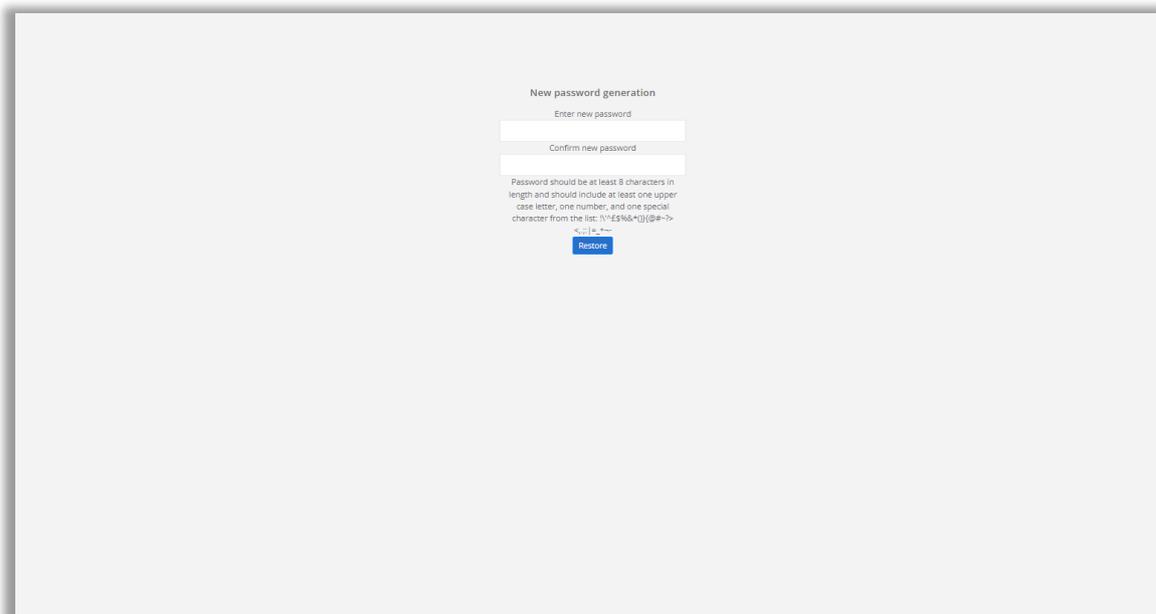


Figure 18. OSIS Ovary access password reset screen.

6.7. Processing a case

To process a case, you must follow the steps described in section 4 (WORKFLOW).

6.8. View the results of a case

If you do not have a user profile with site manager privileges, you will only be able to access a patient report directly from SIVIS via a link in the actual application. If you need assistance with this matter, you will need to open an incident on the IVI Group's incident platform (<https://ivirma.cloud.invgate.net/portal>) to request technical assistance.

If you are a site manager, you can access the list of patients (Figure 19) by clicking on "List of patients".

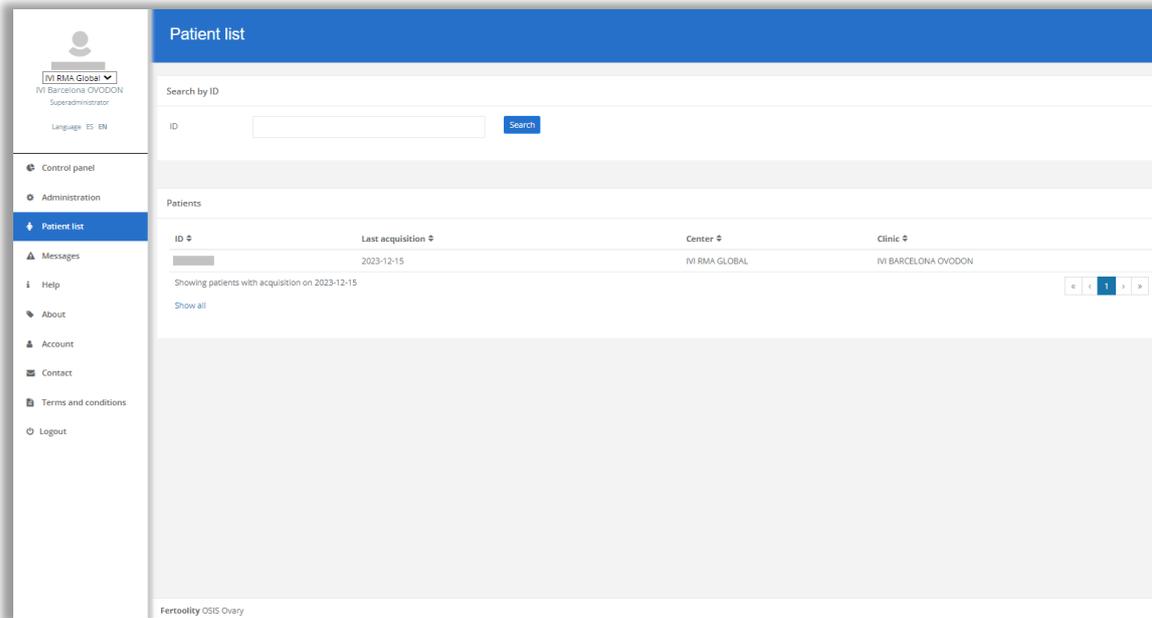


Figure 19. List of patients.

From this screen you can browse the patient table to find the MRN of the patient you wish to consult or enter the MRN in the "Search by NHC" box and click on the "Search" button.

You can enter the patient's full MRN (8 digits) or enter a partial number for the platform to search for all MRNs starting with the digits entered in the box.

Once you have located the patient, click on their MRN to access the patient report screen (Figure 20).

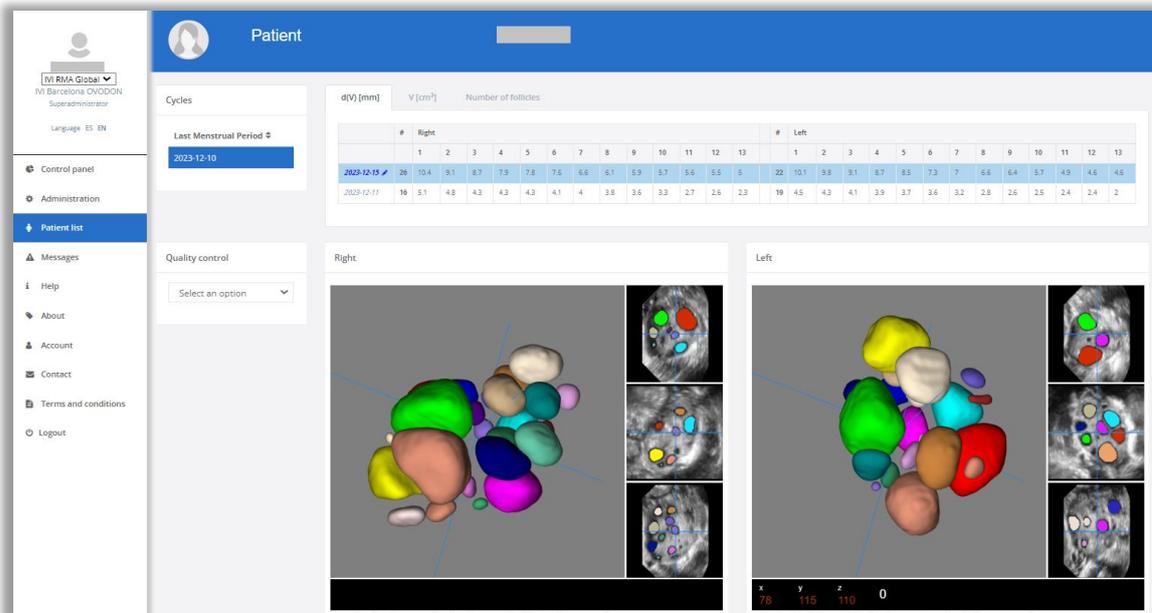


Figure 20. Patient information screen.

On the patient report screen, you can select a stimulation cycle (if there is more than one) in the top left box labelled "Cycle" by clicking on the Last Menstrual Period (Figure 21).

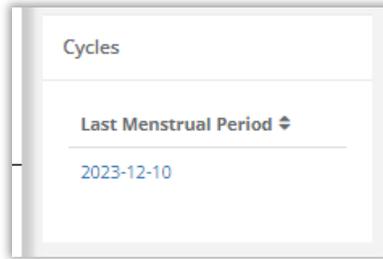


Figure 211. Stimulation cycle table.

Once the stimulation cycle has been selected, a table with follicular diameter $d(V)$, follicular volume and number of follicles will be displayed in different tabs. The rows of the table give access to the different acquisitions (ultrasound scans) that have been performed on the patient during the cycle to date. On this table, each row corresponds to an acquisition in which the above-mentioned information is displayed. The "Right" column corresponds to the right ovary, the "Left" column corresponds to the left ovary and the "#" column indicates the number of follicles detected in that ovary, from highest to lowest (from left to right).

You can click on the acquisition date (Figure 22) to select the one you wish to view (the system selects the latest by default). Once selected, the system highlights the row in blue and displays the automatic segmentation of the patient's follicles in the lower "Right" and "Left" boxes, corresponding to the patient's two ovaries.

d(V) [mm]	V [cm ³]	Number of follicles					
	#	Right					
		1	2	3	4	5	6
2023-12-15	26	10.4	9.1	8.7	7.9	7.8	7.6
2023-12-11	16	5.1	4.8	4.3	4.3	4.3	4.1

Figure 222. Selected acquisition date.

The main view of the multiplanar reconstruction viewer (Figure 23) displays the 3D representation of the automatic segmentation of the follicles present in each ovary (you can move it by clicking and dragging the mouse over the 3D representation). In addition, it shows you the 3 acquisition planes, Sagittal, Coronal and Axial with the automatic segmentation superimposed. You can swap these planes in the main view (which is the largest square) by clicking on the "Swap view" button in the viewer.

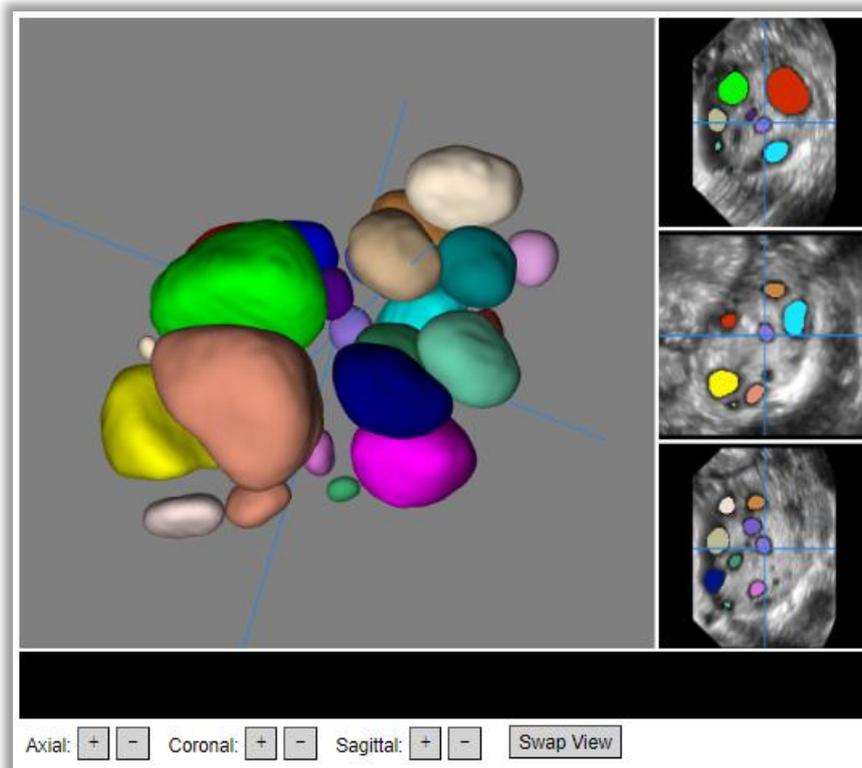


Figure 233. OSIS Ovary multiplanar viewer.

With the mouse over one of the three acquisition planes, you can use the mouse wheel to scroll through the volume slices. You can also scroll through the planes using the "+" and "-" buttons on the viewer (Figure 23) when an acquisition plane is displayed in the main view. The blue axes superimposed on the acquisition planes and represented in the 3D view show the same pixel so that the user can compare the corresponding area between the 4 views.

6.9. Performing quality control of a case

On the patient report screen (Figure 20), after selecting a stimulation cycle in the "Cycle" box and an acquisition (ultrasound) in the "Mean Follicular Diameter" table, you can select one of the options in the lower left box "Quality Control" (Figure 24) referring to the quality of the ultrasound images and results. Once you have clicked on "Save" and confirmed the operation, you will no longer be able to modify the selection. If you have reviewer, administrator or super administrator permissions, you can revert the quality control selection by pressing the "Undo" button.

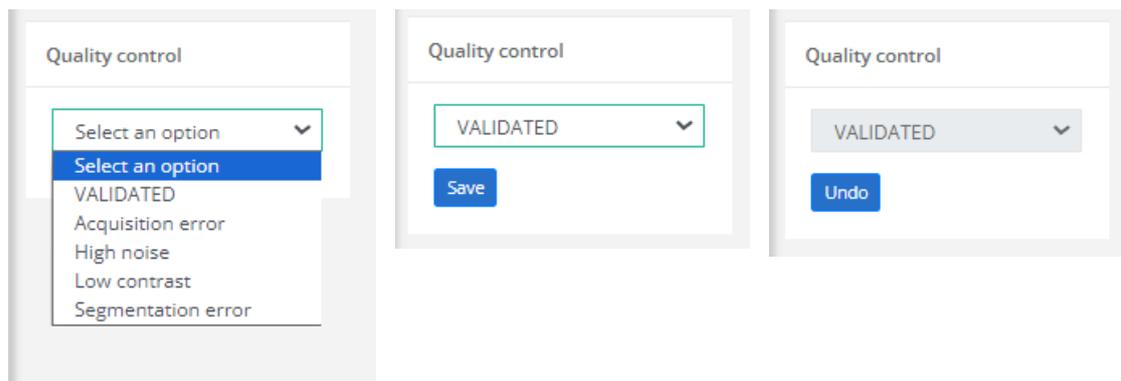


Figure 244. Quality control options.

If you conclude that the images (ultrasound scans) are of sufficient quality, the automatic follicle segmentation is correct and the mean diameter values are adequate, you can select the VALIDATED option in the quality control menu.

If, on the other hand, you consider that the results are not correct due to poor image quality, you can select one of the following options in the quality control menu to state the reason. Figure 25 shows examples of images of insufficient quality:

- VALIDATED: Both segmentation and diameter values are correct.
- Acquisition error: If any of the images (ultrasound scans) do not contain an ovary.
- Excessive noise: If any of the images (ultrasound scans) present too much noise to be able to distinguish the follicles.
- Low contrast: If any of the images do not show enough contrast to distinguish the follicles.
- Segmentation error: If the quality of the images is adequate but the automatic segmentation is incorrect, you can consider a manual correction of the values in the table (explained in the following section).

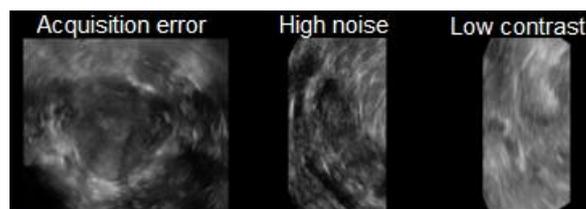


Figure 255. Example of poor-quality images. From left to right, image of a uterus, image with too much noise, image with too low contrast.

6.10. Manually correcting the folliculometry of a case

If the values generated by OSIS Ovary are not sufficient, you can consider a manual correction of these values.

To do this, first select the acquisition you wish to modify (make sure it is highlighted in blue as shown in Figure 20). The acquisition date will appear in bold with a pencil icon next to it indicating that the values can be edited (Figure 22).

Click again on the acquisition date and you will be taken to the manual correction screen (Figure 22).

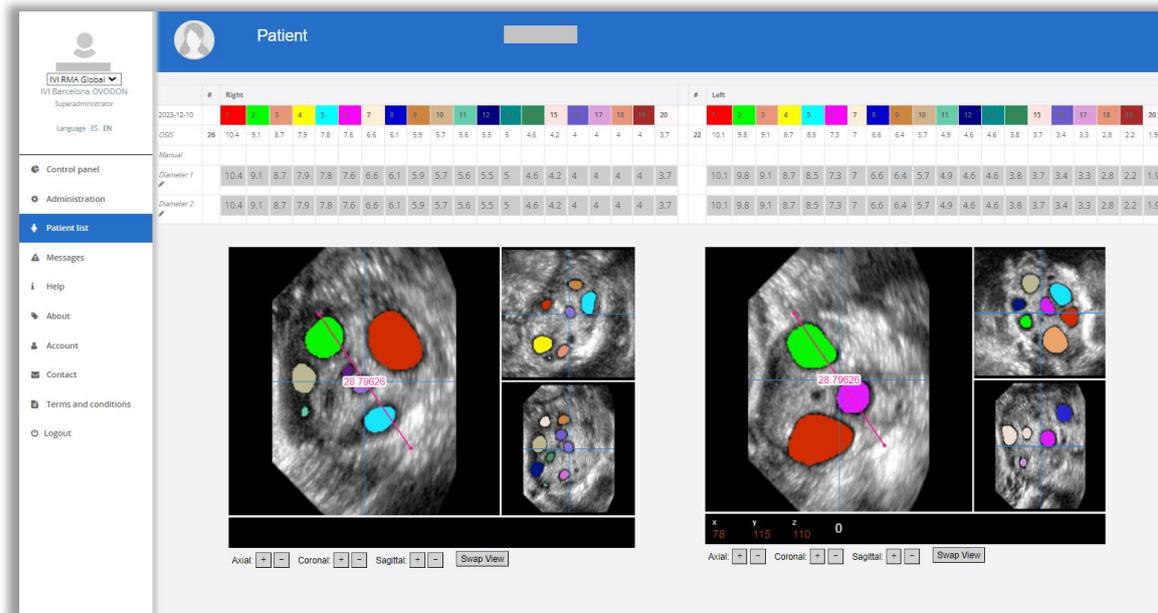


Figure 6. Manual folliculometry correction screen.

The screen is similar to the patient results report, but, this time in the upper table where the d(V)'s are displayed, each follicle is assigned a colour that matches that of the segmentation of that follicle in the multiplanar representation below showing the three acquisition planes (axial, sagittal and coronal) with the segmentation superimposed and a ruler with two adjustment points.

The table of mean diameters has five rows. The first row indicates each follicle's number and its colour. The other rows indicate the following information:

- OSIS: Displays the diameters obtained automatically by OSIS Ovary.
- Manual: Displays the values of the last manual correction if any. When you access the editor again after saving your manual correction, you will be reminded of the result in this row.
- Diameter 1 and Diameter 2: These are editable boxes which, when the screen opens, show the automatic values obtained by OSIS Ovary to facilitate the task. In these boxes the diameters measured with the ruler tool on the multiplanar viewer will be entered.

On this screen you can take diameter measurements manually. The steps are as follows:

1. Identify the colour of the follicle you need to correct (e.g., red).
2. Navigate the display until the follicle to be measured is located (Figure 26).
3. Select a slice where the diameter can be clearly measured (Figure 26). Note that for the measurement to be representative, you should select two planes where the diameter is at its maximum.
4. Adjust the ends of the ruler by dragging them to the contour of the follicle to be measured (Figure 26).
5. Write the value provided by the ruler in the Diameter 1 box of the follicle to be corrected. If you are measuring a follicle that has already been detected, you should overwrite its previous value in the box. If, on the other hand, you are measuring an undetected follicle in order to add it, enter it in one of the empty boxes.
6. Repeat steps 3, 4 and 5 to obtain another measurement to be entered in the Diameter 2 box of the follicle to be corrected.
7. When you have noted down the measurements for all the follicles you wish to correct, click on the "Save" button at the bottom (Figure 27).

You must enter two measurements for each follicle you wish to correct. If a measurement has been missed, the system will remind you with an error message next to the "Save" button with the text "You must enter two values per follicle". From these measurements, the system will calculate the average and save it.

If you want to remove a follicle (e.g., the green one), leave its Diameter 1 and Diameter 2 boxes blank as shown in Figure 26.

	#	Right		
2023-12-10	1			4
OSIS	26	10.4	9.1	7.7
Manual				
Diameter 1		10.4		7.7
Diameter 2		10.4		7.7

Figure 267. Blank boxes to delete a follicle.

When you click on save, the system will read the data entered in the Diameter 1 and Diameter 2 boxes, compute the mean value for each diameter by calculating the average of the two diameters entered (formula 1) and store it for display in the patient report.

$$\text{Mean diameter} = \frac{\text{Diameter 1} + \text{Diameter 2}}{2} \quad (1)$$

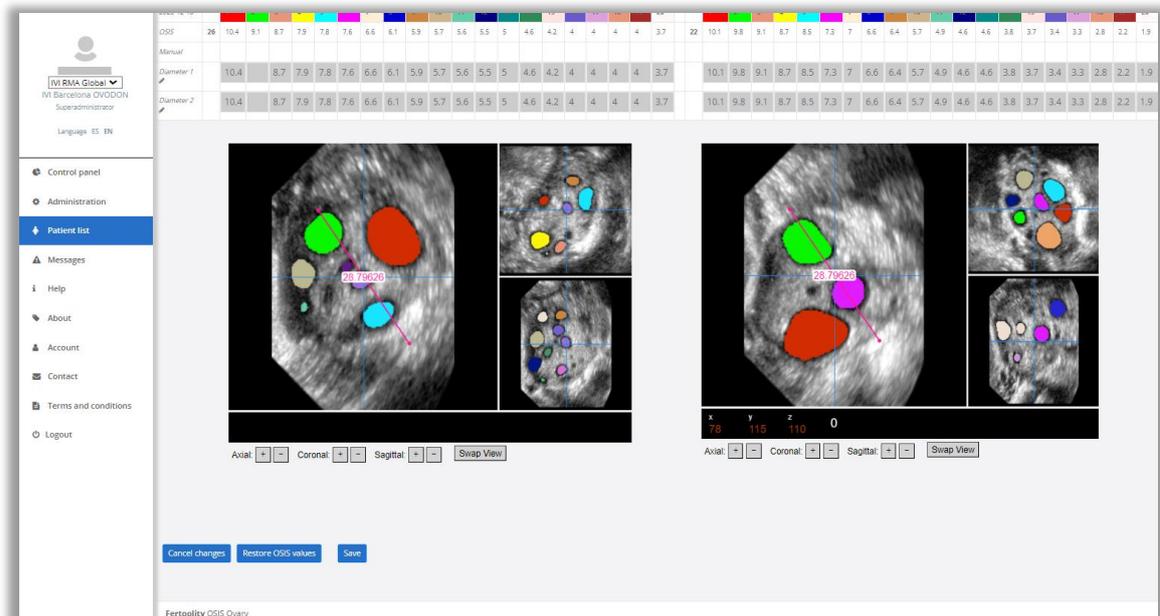


Figure 278. Manual folliculometry correction screen (buttons).

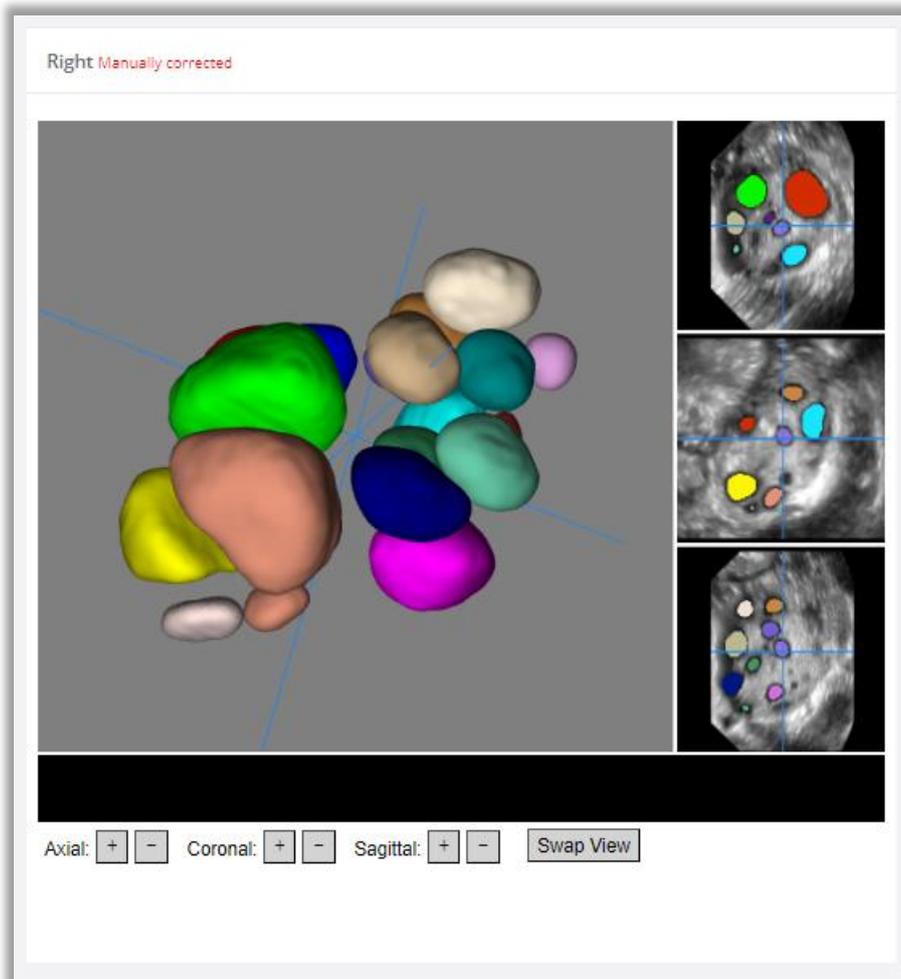


Figure 289. Multiplanar display in the patient report after manual correction.

If during the correction process you want to discard the changes made and return to the patient report, click on the "Cancel changes" button.

If you wish to revert the values of a manual correction that has already been saved and restore the automatic OSIS Ovary values (the values before the manual correction was performed) click on the "Restore OSIS values" button.

6.11. Manage clinics and centre users (Administrator)

If you are an administrator, a new option will appear in the side menu (Figure 13) under the name "Administration" (Figure 30) where you can consult the licence contracted by your centre in the upper table "Licence", the ultrasound machines registered in the system in the table "List of clinics", and the users who have been given access to the platform in the table "List of users".

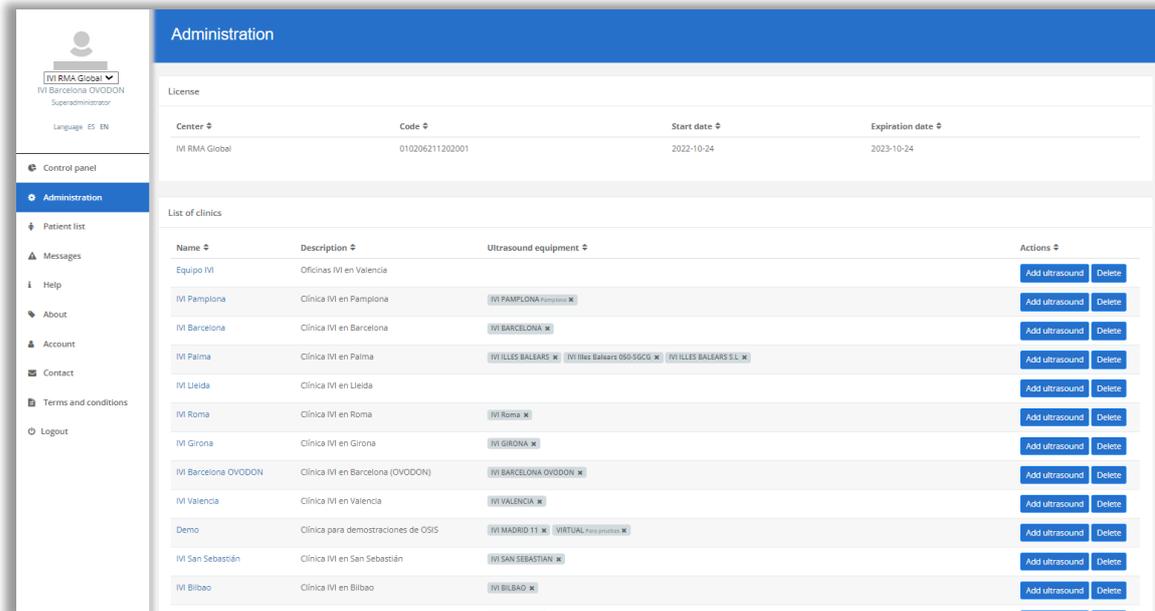


Figure 30. Administration screen.

Consulting licences:

In the "Licences" table you can check the licence status of your centre. This includes the licence code, the start date and the end date of the licence.

Administration of clinics and ultrasound machines:

In the table "List of clinics" you will find a list by rows of all the clinics registered to your centre identified by name and description as shown in Figure 30.

The "Ultrasound machines" column contains a list of ultrasound machines associated to each clinic and displayed as labels with the name and description (if any) of each registered ultrasound machine, as well as an "X" which you can click to delete the corresponding ultrasound machine, in the event you wish to deconfigure it.

In the "Actions" column you will find two buttons associated to each clinic: The first one, "Add ultrasound machine" will allow you to open a dialogue to enter a new ultrasound machine for the corresponding clinic by entering the machine's identifier and a description (see Figure 31). This identifier corresponds to the HOSPITAL parameter of your ultrasound machine. Contact the technician at your centre or clinic to access this configuration or our technicians by sending an email to info@fertoolity.com.

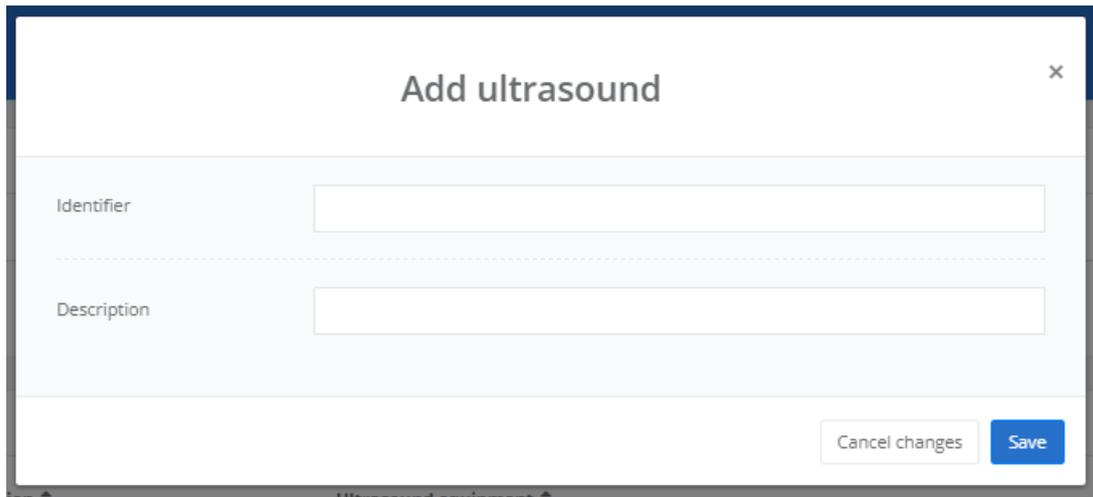


Figure 31. Dialogue to add an ultrasound machine to a clinic.

The second button you will find in the "Actions" column is the "Delete" button, which will allow you to delete a clinic after confirming the action in a dialogue. Please note that the application will not allow you to delete clinics that have users or patients registered in them for security reasons.

User administration (Administrators):

In the "List of users" table you will find a list of all the users registered at your centre identified by the columns "Name", "Surname" and "E-mail" (Figure 32).

First name	Last name	E-mail	Status	Role	Clinic	Actions
[Redacted]	[Redacted]	[Redacted]	Active	Superadministrator	Equipo IVI X	Add clinic, Delete
[Redacted]	[Redacted]	[Redacted]	Active	User	Equipo IVI X	Add clinic, Delete
[Redacted]	[Redacted]	[Redacted]	Active	Reviewer	Equipo IVI X	Add clinic, Delete
[Redacted]	[Redacted]	[Redacted]	Active	Reviewer	Equipo IVI X	Add clinic, Delete
[Redacted]	[Redacted]	[Redacted]	Active	Reviewer	Equipo IVI X	Add clinic, Delete

Figure 32. List of users.

In the "Status" column you will see an indicator with two possible positions, "Active" when the user can access the platform or "Blocked" when the user is not allowed to access the platform. By clicking on the status, you can toggle between Active and Blocked. In addition, when a user enters their password incorrectly too many times, the platform blocks their access for security reasons.

In the "Role" column, the user's role or privilege level will appear. As long as the user is not a Super Administrator, the role can be modified by clicking on the drop-down menu and selecting a new value.

The "Clinics" column shows a list of all the clinics to which the user is linked. This link allows you to view patients from that clinic. Each clinic appears as a label with the name of the clinic and an "X"

that will allow you to disconnect the user from that clinic. Please note that the application will not allow you to delete a user's last clinic.

Finally, in the "Actions" column you will find two buttons: The "Add clinic" button will allow you to link the user to a new clinic. By clicking on the button, a dialogue will open with a drop-down menu where you can select the clinic (Figure 33). Finally, the "Delete" button will allow you to remove the user from the list.

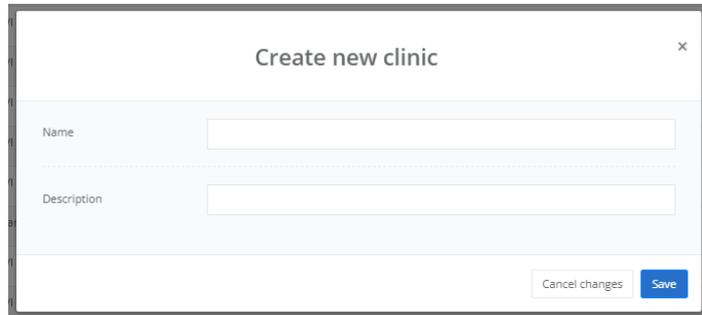


Figure 29. Dialogue to link user to clinic.

If you need to assign Super Administrator privileges to one or more users you can contact the Fertoolity team by sending an email to info@fertoolity.com.

At the bottom of the table, you will find the "Create new user" button which will open a dialogue to create a new user account as shown in Figure 34. In this dialogue you will have to enter a valid e-mail address belonging to the new user to which a confirmation e-mail will be sent for them to set their password. You will also need to enter the user's first name and surname, assign a role (privileges) and select a clinic to which the user will be linked to start with.

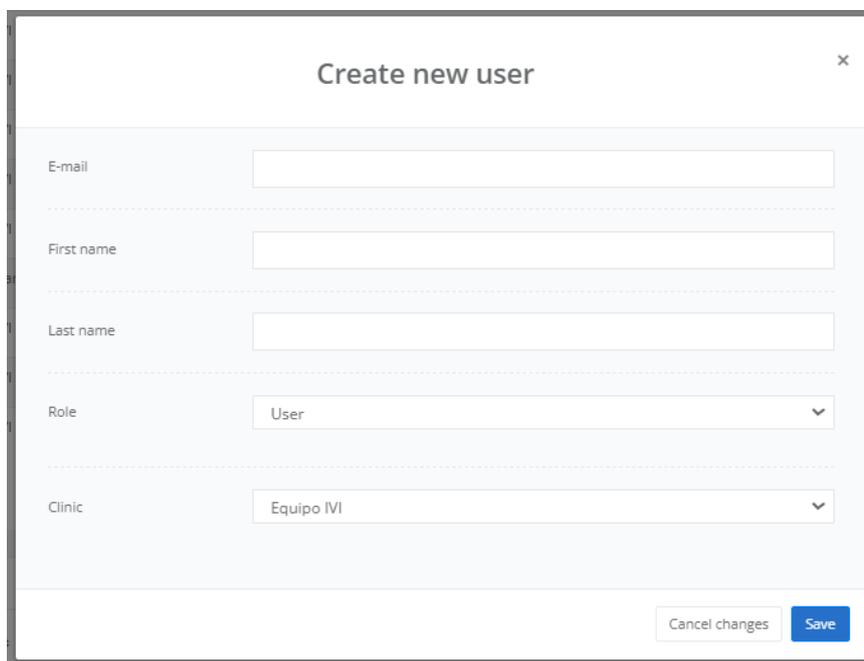


Figure 30. User creation dialogue.

6.12. Log out

To log out, click on the "Log out" button on the side menu (Figure 13). We strongly recommend that you do not leave your workstation without logging out of the active session on the platform.

This option is valid whether you are logged in from SIVIS or directly from the Login screen.

7. POSSIBLE ERRORS

It is possible that an error may occur during the process of exporting or generating results. Whenever it is possible to retrieve the information, the system will display an error message in the "Messages" section. If you submit a case to OSIS Ovary and after some time it does not appear in the list of patients, please contact the technician at your centre or clinic or contact us at info@fertility.com to identify the cause of the problem.

OSIS Ovary will log these errors with as much information as possible and display them to the user on the platform in the "Messages" section (Figure 33) available on the side menu (Figure 13).

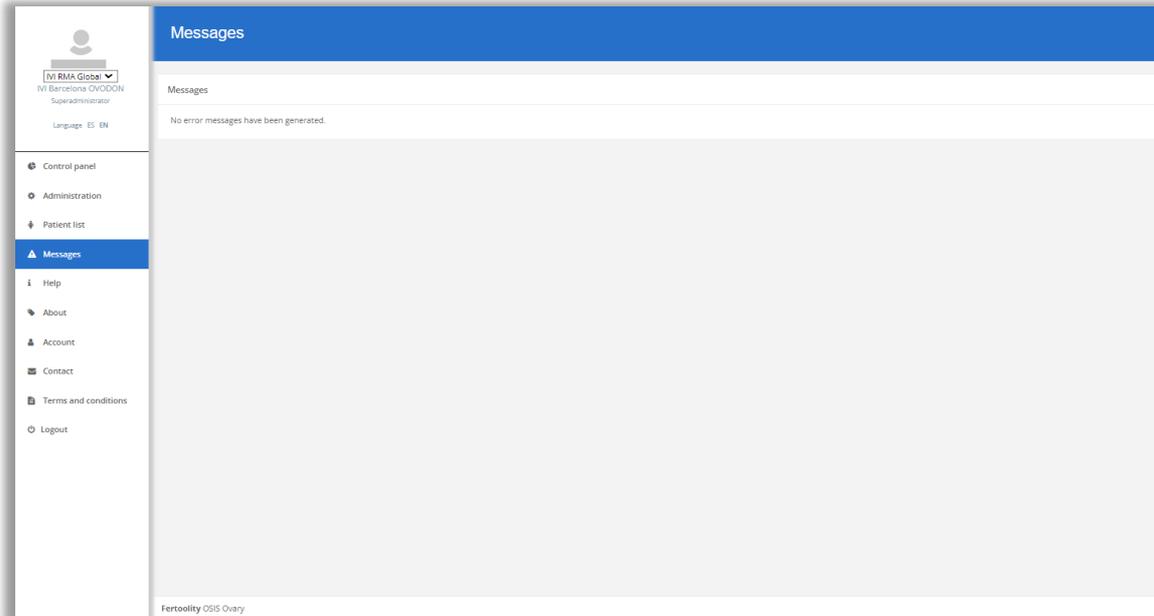


Figure 31. Error message screen.

When OSIS Ovary detects an error, the icon in the "Messages" section will appear in red. Click on the "Messages" option to access and read any errors that may have occurred.

In the "Messages" table, a list of the last unread error messages will be displayed. Once read, when you exit the screen, they will not appear again and the icon in the side menu will change from red to grey.

For each error we observe the following fields:

- Date: Date on which the error was generated.
- MRN: MRN of the patient whose case generated the error (if it was possible to retrieve it).
- File: Name of the file that generated the error.
- Message: Description of the error and a recommendation to fix the problem. The error description appears in red the first time it is read.

After following the recommendations, if the error persists, please contact the Fertility team by sending an email to info@fertility.com indicating all the details of the error listed in the table.

The following are the possible errors that OSIS Ovary is able to detect, with a brief description of each and the actions to be taken by the user:

1. **File cannot be processed:** OSIS Ovary has received a file in a format that it cannot process. The user will have to re-export the case from the ultrasound machine following the instructions in section 4 of this manual, Workflow.
2. **Incorrect MRN for the file received:** The system reports the reception of a volume with an incorrect MRN (without the eight digits it should contain). In these cases, it is therefore impossible to identify the patient. The way to solve this is to re-edit the volume in the ultrasound machine, and re-enter the correct MRN and export the volume (previously saved) from the ultrasound machine again.
3. **No valid images found (images must be 3D volumes):** The system reports the incorrect format of processable files for OSIS Ovary. In these cases, the user must export the ultrasound volumes again, but in “.vol” format.
4. **No acquisitions found:** No ultrasound file has arrived in the OSIS Ovary system, but the associated data has arrived. This may be due to two causes: either the Internet connection failed for a few seconds (and therefore the file is incomplete or corrupted and not received) or the option "create patient/examination folders" was not selected prior to export, or the file did arrive at OSIS Ovary, but it is located in the server's bin, and therefore is not indexable, and is not detectable. In these cases, the user should export the ultrasound volumes again as explained in section 4 (Workflow) of this manual, as well as contact the clinic's IT maintenance services to check that the network connections are working properly.
5. **Patient data not included in the export:** Patient data have not arrived with the exported image. In this case, the user must export the ultrasound volumes again as explained above.
6. **Incorrect image name:** The images that have arrived at OSIS Ovary are not named correctly and, therefore, it is not possible to identify which one corresponds to the right ovary and which one to the left. You should contact your centre manager or the Fertoolity team to solve this problem.
7. **An error occurred during image analysis:** Fault in the file handling process and/or automatic analysis. Contact the Fertoolity team for a thorough review.
8. **Ultrasound identifier received is not registered:** OSIS Ovary has not registered the identifier under which your ultrasound machine sends cases to the platform. This may be because your ultrasound machine's configuration has been changed or your centre's manager has not registered your ultrasound machine. Please contact the Fertoolity team so that they can review your case carefully.

It is possible that neither the exported ultrasound volume file nor the accompanying data will reach OSIS Ovary. In this case, OSIS Ovary will obviously not be able to report this fault to the user. If this happens, contact the Fertoolity team to identify the cause of the problem.

8. OSIS Ovary SECURITY MEASURES

8.1. Authentication options

OSIS Ovary supports token-validated registration by email. Emails are checked to prevent re-use, spam or malware emails, and other security issues.

8.2. Secure storage of credentials

OSIS Ovary follows secure credential storage best practices by never storing regular passwords, and only irreversible hashes using SHA3 are stored. Fertoolity employees cannot access credentials even in the event of a data breach.

8.3. Secure credential policies

Each OSIS Ovary user sets their own password according to the following password policies:

- At least 8 characters in length.

- At least one lower case character.
- At least one upper case character.
- At least one number
- At least one special character

All credentials are only stored as a hash and it is not possible to access the full password.

8.4. Security and authentication

Users are authenticated by their username (which is their e-mail address) and password. The password is transferred encrypted from the user's computer to the server making it impossible to recover in case of interception of the transfer.

8.5. Security vulnerabilities

Security issues such as the OWASP (Open Worldwide Application Security Project) top 10 vulnerability issues are covered by our use of security frameworks and measures such as same-origin policies and SQL (Structured Query Language) injection protectors.

8.6. Additional product security features

8.6.1. Access privileges and roles

Access to data within OSIS Ovary is governed by access rights and can be configured to define access privileges. OSIS Ovary has several permission roles: User, Reviewer, Administrator and Super Administrator. Table 1 lists the functionality each role has access to.

Table 1: Access to OSIS Ovary functionalities by user role

User role	Functionalities
User	<ol style="list-style-type: none"> 1. Change language 2. Messages: Access to error messages 3. Help: Access to these instructions for use and change log 4. About: Access to the product label 5. Account: Accessing account information, language change and password change 6. Contact: Contact link by e-mail. 7. Terms and conditions: Consulting the platform's terms and conditions of use. 8. Logout: Close the open user session. 9. Access to patient report via link from SIVIS 10. Access to make manual corrections to a patient report. 11. Access to select an option in quality control.
Reviewer	<ol style="list-style-type: none"> 1. All accesses of the "User" role 2. List of patients: Consulting and searching for patients on the platform. 3. Possibility to revert a saved quality control on a patient report.
Administrator	<ol style="list-style-type: none"> 1. All accesses of the "User" and "Reviewer" roles. 2. Administration: Access to clinic creation and ultrasound machine management. Access to the creation of user accounts and administration of their access and user role. Access to the contracted licence.
Super administrator	<ol style="list-style-type: none"> 1. All access for the "User", "Reviewer" and "Administrator" roles. 2. Change of centre.

	<p>3. Control panel: Access to the current server utilisation percentage and free storage space. Access to a summary of the centres registered on the platform. Access to the UDI code and the possibility of modifying it to generate a new one. Access to the user access log.</p>
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8.6.2. User provisioning

Adding and editing users can be carried out manually by the Fertoolity team.

8.6.3. Transmission security

All communications with OSIS Ovary's service provider servers are encrypted using industry standard HTTPS (HyperText Transfer Protocol Secure). This ensures that all traffic between you and OSIS Ovary is secure in transit.

OSIS Ovary is designed to be integrated into the IVI RMA Group's clinic computer system. Therefore, in addition to the measures described above, the IVI RMA Group implements protection mechanisms in the clinics' own network so that OSIS Ovary is not affected by security problems. These mechanisms are as follows:

1. Vulnerability analysis
2. 24-h network monitoring
3. Troubleshooting
4. Accident response
5. Desktop support
6. Alert system
7. Protection with Azure Sentinel

In addition to these measures, the health sector good practices recommended by the European Union are complied with:

1. General Data Protection Regulation (GDPR)
2. Network and Information Security Directive (NIS Directive)
3. European Union Cybersecurity Act

A Perimeter Protection System, which protects OSIS Ovary, is also implemented at IVI RMA:

1. Cisco Umbrella
2. Fortinet firewalls
3. Windows Defender
4. Multi-factor authentication.

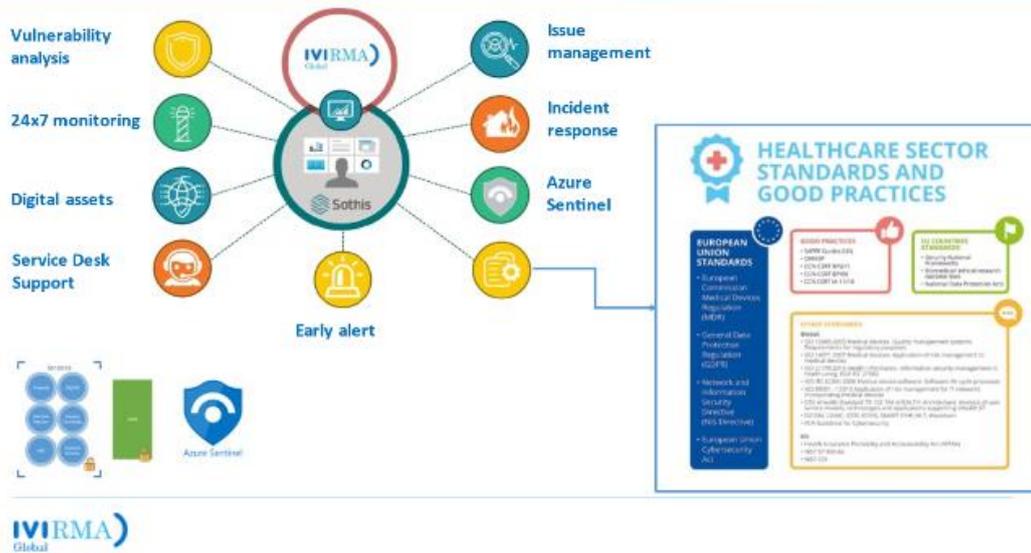


Figure 32. Outline of Cybersecurity measures implemented by IVI RMA Global at OSIS Ovary.

9. PERFORMANCE OSIS Ovary

9.1. Accuracy

OSIS Ovary reports an accuracy of 90% for automatic segmentation and a concordance against Ground Truth in clinical practice of 80% for follicle detection and mean diameter measurement.

Staying within this percentage requires specific training in the use of ultrasound machines and special attention to the quality of the images acquired.

9.2. Quantification

OSIS Ovary calculates the number and size of follicles in each ovary by automatically segmenting them using an artificial intelligence algorithm. This measurement process is called quantification and is carried out as follows:

- **Number of follicles:** number of independent segmented elements in the ovary calculated from the grouping of pixels corresponding to the interior of a follicle that are adjacent to each other.
- **Follicular volume:** For each follicle, the voxels that make up the follicle are counted. This count is multiplied by the volume in cubic centimetres of each voxel, which is given by the image resolution (obtained from the image analysed).
- **d(V) or Relaxed sphere diameter:** The diameter corresponding to a perfect sphere is calculated with the volume measured for each follicle. The following formula is used for this purpose:

$$d(V) = \sqrt[3]{\frac{6 * volume}{\pi}}$$