Med-Imaps SA
PTIB
Hôpital Xavier Arnozan
Avenue du Haut-Lévêque
F – 33600 PESSAC
Tel. +33 (0)5 57 10 28 56
www.med-imaps.com

TBS CALCULATOR

USER GUIDE

User Guide version 2.0
This User Guide is based on TBS Calculator version 2.0

Société Anonyme au capital de 461 120€
RCS Bordeaux 491 084 216 000 10

Table of contents

I. Overview

A. Intended use

TBS Calculator is a software intended for use as an investigational tool only.
It computes the antero-posterior spine DXA examination files and calculates a score: Trabecular Bone Score (TBS). The TBS is derived from the texture of the DXA image and has been shown to be related to bone microarchitecture and fracture risk. This data provides information independent of BMD value.

B. Prerequisites

TBS Calculator is intended to be installed on a PC with a configuration equal to or higher than:

- Processor: 1 GHz;
- RAM: 1 GB;
- Disk space: 1GB free;
- Operating system: Windows XP, Windows Vista or Windows 7.

C. Input data

The software is able to analyze scans from several devices. All most recent scanners from GEHC Lunar and Hologic companies are compatible with TBS Calculator.

1. Compatible devices

Manufacturer	Model
GEHC Lunar	iDXA
GEHC Lunar	Prodigy
GEHC Lunar	Prodigy Compact
GEHC Lunar	Prodigy Pro
GEHC Lunar	Prodigy Pro Compact
GEHC Lunar	Prodigy Advance
GEHC Lunar	Prodigy Advance Compact
GEHC Lunar	Prodigy Primo
GEHC Lunar	Prodigy Primo Compact
HOLOGIC	Discovery A
HOLOGIC	Discovery C
HOLOGIC	Discovery W
HOLOGIC	Discovery SL
HOLOGIC	Discovery Ci
HOLOGIC	Discovery Wi
HOLOGIC	QDR 4500 A
HOLOGIC	QDR 4500 C

HOLOGIC	QDR 4500 W
HOLOGIC	QDR 4500 SL
HOLOGIC	Delphi A
HOLOGIC	Delphi C
HOLOGIC	Delphi W
HOLOGIC	Delphi SL

2. Compatible DXA software

TBS calculator has been validated for the analysis of the DXA scan files created by the following DXA software:

- GEHC Lunar - enCORE, versions 8.0 to 14.1
- Hologic QDR Workstation, versions 12.3 to 12.7
- Hologic APEX, versions 1.0 to 4.0

3. Data source

The scans to be analyzed must be stored in specific folders. In each folder, scans must originate from the same center and the same DXA scanner.

D. TBS calculation

TBS is calculated using a specific algorithm that is optimized for each scanner model.
In order to be able to compare TBS values calculated from scans acquired on different scanners, a X-calibration must be done.
This X-calibration is a linear correction that will be applied on TBS output values. It is defined by a slope and an intercept value. By default, those parameters are, respectively, set to 1 and 0 in the software. They should be modified by the user if he intends to calculate TBS score on data providing from different scanners.

E. Output data

TBS Calculator software stores the calculated TBS values in a Microsoft Excel compatible file (CSV formatted). This file contains one row per scan and the following columns:

- Scan date
- Scan mode
- BMD analysis date
- TBS analysis date
- Patient ID
- Patient's First name
- Patient's Last name
- Patient's height
- Patient's weight
- Patient's Body Mass Index
- Patient's date of birth
- Patient's age
- Patient's sex
- Patient's ethnicity
- L1 BMD (g/cm^2) – If not measured, "N/A" is displayed

- L2 BMD (g/cm²) – If not measured, “N/A” is displayed
- L3 BMD (g/cm²) – If not measured, “N/A” is displayed
- L4 BMD (g/cm²) – If not measured, “N/A” is displayed
- Mean BMD Spine (g/cm²) = $\Sigma(BMD_i x Surface_i)/\Sigma(Surface_i)$ of measured and not excluded ROI
- L1 TBS – If not measured, “N/A” is displayed
- L2 TBS – If not measured, “N/A” is displayed
- L3 TBS – If not measured, “N/A” is displayed
- L4 TBS – If not measured, “N/A” is displayed
- Mean TBS Spine (of measured and not excluded ROI)
- L1 measured – TRUE or FALSE
- L2 measured – TRUE or FALSE
- L3 measured – TRUE or FALSE
- L4 measured – TRUE or FALSE
- L1 excluded – TRUE or FALSE
- L2 excluded – TRUE or FALSE
- L3 excluded – TRUE or FALSE
- L4 excluded – TRUE or FALSE
- L1 Surface (cm²) – If not measured, “N/A” is displayed
- L2 Surface (cm²) – If not measured, “N/A” is displayed
- L3 Surface (cm²) – If not measured, “N/A” is displayed
- L4 Surface (cm²) – If not measured, “N/A” is displayed

---------- GE-Lunar devices only ----------

- Combined Spine vertebra – For ex. “L1-L4”
- L1 BMD T-score – If not measured, “N/A” is displayed
- L2 BMD T-score – If not measured, “N/A” is displayed
- L3 BMD T-score – If not measured, “N/A” is displayed
- L4 BMD T-score – If not measured, “N/A” is displayed
- Combined Spine BMD T-score – If there aren’t 2 adjacent vertebra available, “N/A” is displayed
- L1 BMD Z-score – If not measured, “N/A” is displayed
- L2 BMD Z-score – If not measured, “N/A” is displayed
- L3 BMD Z-score – If not measured, “N/A” is displayed
- L4 BMD Z-score – If not measured, “N/A” is displayed
- Combined Spine BMD Z-score – If there aren’t 2 adjacent vertebra available, “N/A” is displayed

---------- End of GE-Lunar devices only ----------

- X-cal Slope
- X-cal Intercept
- Input Folder
- Input File
- Center name
- Study phase
- Device Model
- Device serial number

F. Performances and limits

1. Performance testing

Ex vivo studies carried out from bony pieces of human cadavers have enabled us to assess the exactness of the TBS parameter from statistical correlations established with the Parfitt’s “standard” 3D parameters that characterize the bone microarchitecture. Significant statistical correlations have been established between the TBS parameter and the 3D parameters of connectivity density, intertrabecular spacing and the number of trabeculae. These levels of correlation proved to be stable among several sub-set samples, and strong for independent evaluations lead from several aforementioned bone densitometers.

The reproducibility of the TBS parameter has been assessed according to a standard methodology based on experiments carried out on a set of vertebrae of human cadavers for devices listed in paragraph I.B.1, see page 3.

2. TBS and soft tissues

It is worth remembering that the patient's acquisition must be carried out with the acquisition mode recommended by the manufacturer and corresponding to his/her corpulence. As a consequence, **it is important that his/her weight and height be updated at each examination.**

Warning: In order to escape from the influence of soft tissue in extreme cases, the TBS algorithm takes into account the acquisition mode used for the realization of the DXA examination as well as the patient's BMI based on the values of Weight and Height.

⚠ Erroneous Weight and/or Height values (typing mistake on the part of the operator) may bias the TBS values in an uncontrolled manner; thus, it is recommended to systematically check the exactness of the patient's Weight and Height values reported in the DXA examination;

⚠ With GEHC-Lunar DXA scanners, TBS values computed from scans acquired in thin and thick mode may be biased; thus, **it is recommended not to take into account those values.**

⚠ In extreme cases where patients have a body mass index below 15 kg/m^2 or over 35 kg/m^2, it is possible that the TBS values be biased; thus, **it is recommended not to take into account TBS values for patients with BMI below 15 kg/m^2 or over 35 kg/m^2.**

For the case of a patient of normal corpulence presenting a more significant distribution of fat on the abdomen (case of an android type repartition), the DXA acquisition mode recommended by the manufacturer may be the "Thick" mode whereas the BMI is normal; in this specific case the probability that the TBS values are biased in an uncontrolled manner is high (for example, an excessively low TBS value). Thus, it is recommended to use more often the acquisition mode that is more logically adequate with the BMI value and to switch to the thick or thin modes only when extremely necessary (for example: in doubt about the accuracy of the BMD value for a thickness value of a patient in the excessively high or low acquisition zone).

3. Output standardization

TBS values are standardized so that, whatever bone densitometer brand and model is used, they can be plotted on a unique reference graph.

Thus, average TBS scores produced by all devices and models are identical. Therefore, due to technological differences between the scanner models and brands, **two TBS scores obtained for a patient on 2 different scanner models must not be compared**.

Moreover, **patient follow-up should always be performed on the same bone densitometer.**

G. Regulation

TBS iNsight® is not considered as a medical device since it is intended for investigational use only.

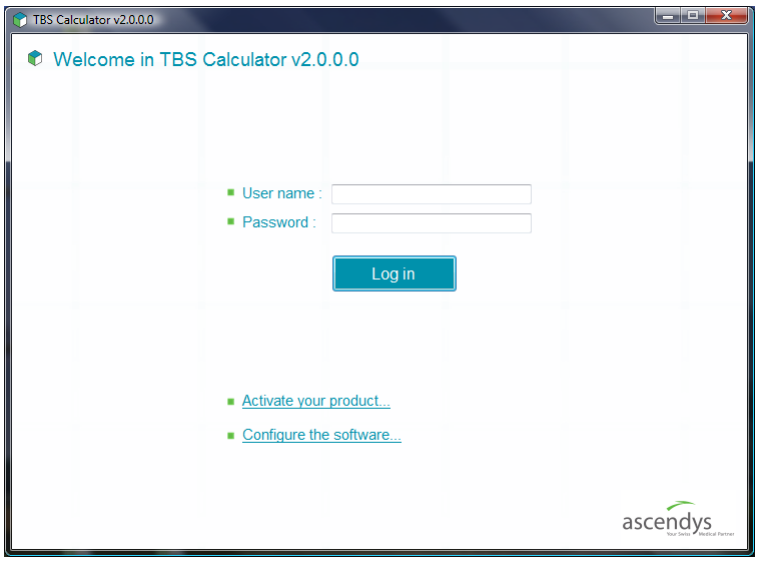
II. How to use TBS CALCULATOR?

A. Software activation

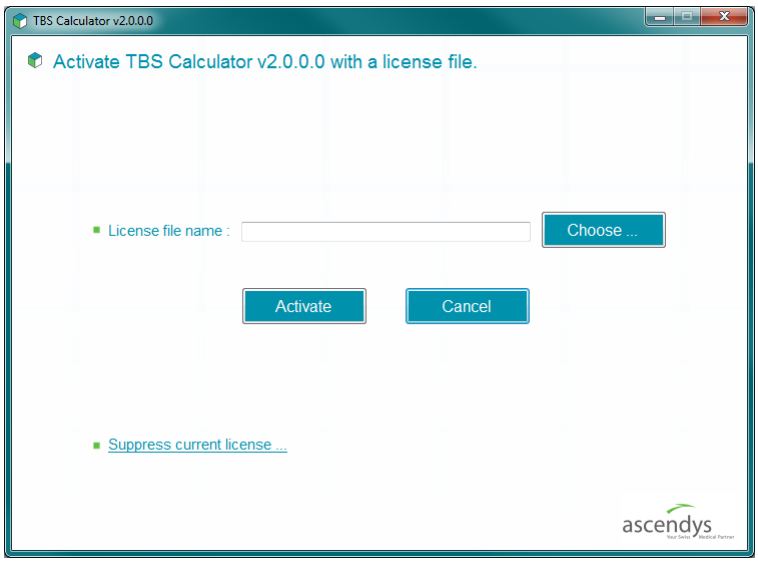
Once installed, the TBS Calculator software must be activated before any DXA scan can be analyzed.
Activation may be done using a specific license file that has to be imported into the software and allows computation of TBS scans from one or several DXA scanners or it may be done online for users that have purchased a permanent web account.

1. Product activation in Research Centers

The software is intended to analyze clinical data of known research centers. It is restricted to some scanners with known serial numbers.
The list of authorized DXA scanners is included within the TBS Calculator license file, which also defines a validity period: it may be unlimited or limited to a couple of months.

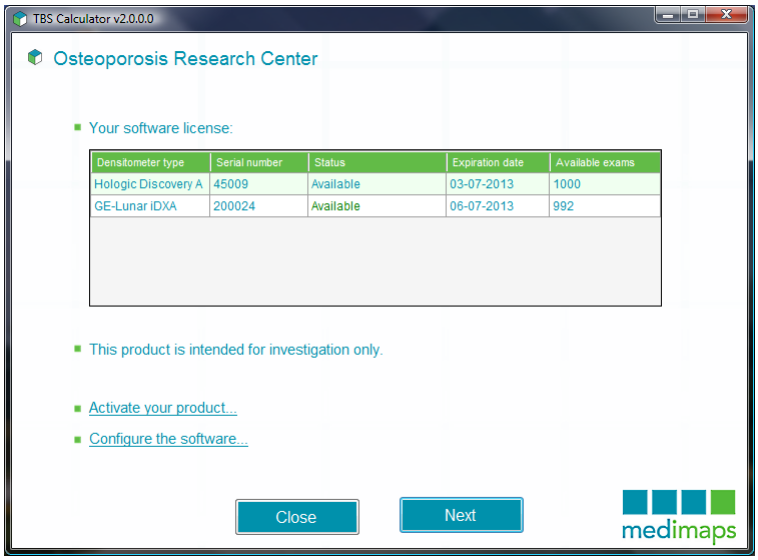


Click on “Activate your product…” in order to import your license.



Click on the Browse button, then select the license file that your retailer has sent you and then click on “Activate”. The list of DXA scanners with corresponding validity period and number of DXA scans that can be analyzed, if limited, is displayed.

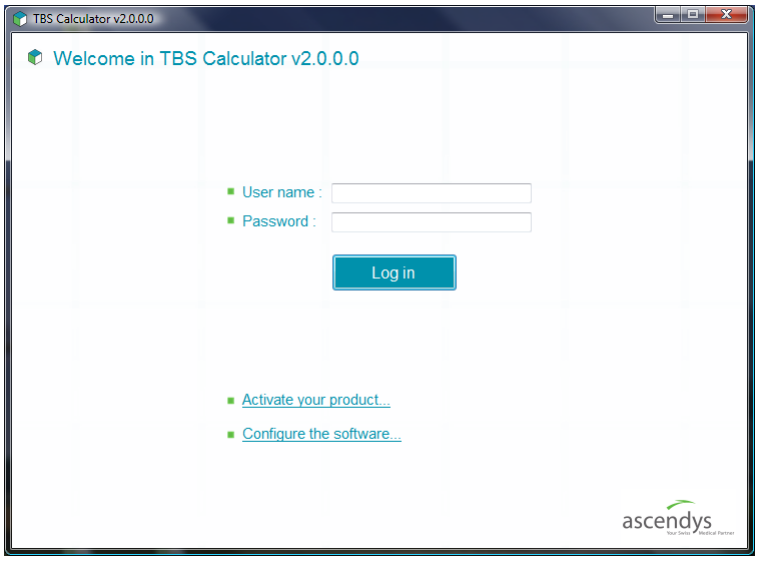
* “Suppress current license…” allows you to switch to online mode (you must have a user account to access online mode)



Then click on “Next” to select the input data folder.

2. Product activation for Contract Research Organization

A specific work mode has been designed for Contract Research Organizations: a connected work mode, where the number of authorized DXA scanners is not limited while the number of analyzed scans is limited as well as the validity period of the analysis.



Enter your user name and password and then click on the "Log in" button in order to be identified by the system.

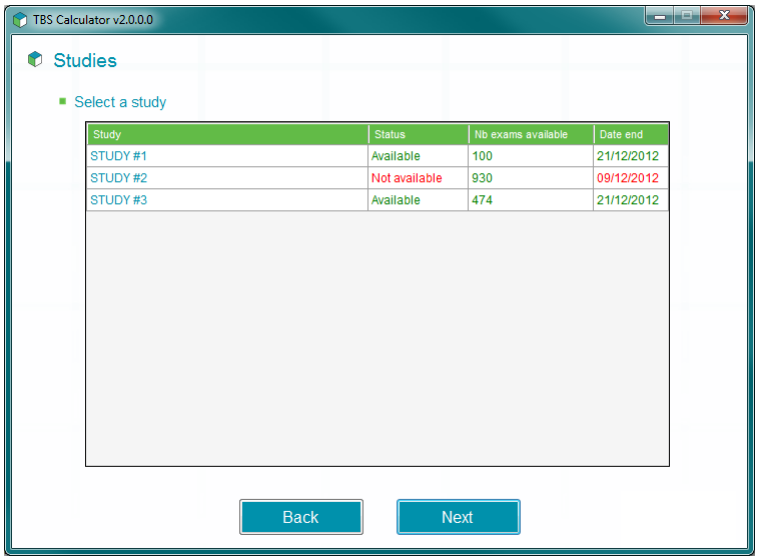
Your computer must be connected to internet when you log in and when you analyze scans.

For each TBS Calculator user, an account in the TBS Calculator web platform is created when the contract is signed. Then for each study signed by the CRO with its clients, a corresponding order must be sent to Ascendys with the following information:

- Study name (an id that will be used to make it possible to analyze the corresponding scans)
- Number of scans to analyze in the study
- Study date start
- Study duration

Then, when you log in, the list of studies will be displayed with the corresponding information:

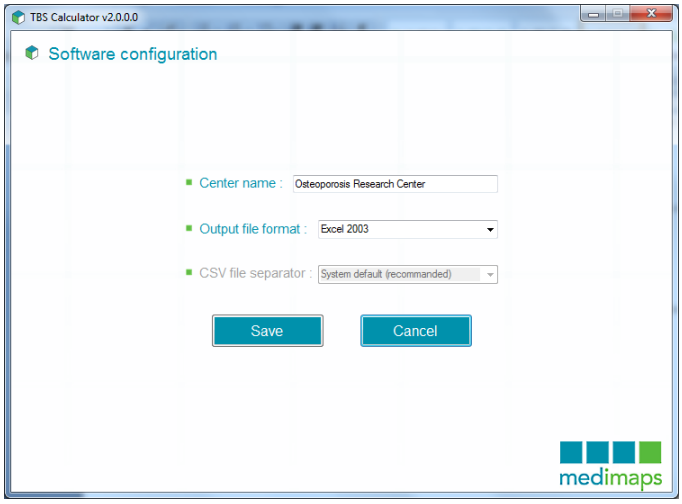
- Study name
- Number of scans analyzable
- Study date ends



Select the study you want to analyze and click Next.

B. Software configuration

The name of the Center or of the company can be displayed in the first page of the software. In order to enter it, please click on "Configure the software...".



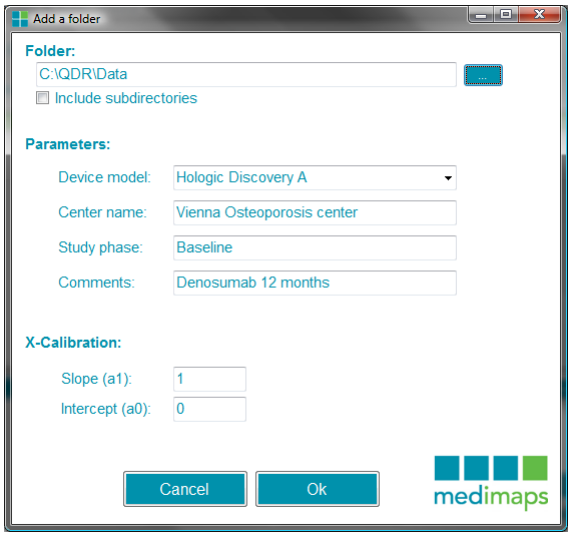
The output data will be populated in a MS Excel compatible file, which can be chosen between Excel 2003 (.xls) and comma separated values (.csv).
If CSV format is selected, the cell separator can be forced to a different value than that configured in Windows operating system.

C. Input data

The scans to be analyzed must be stored in specific folders. In each folder, all the scans must originate from the same scanner.

1. Add folders containing scans

When clicking on the "Add folder" button, a window is displayed where the user must indicate:



- Folder path
- Device model
- Center name (where the scans come from - optional)
- Study phase (optional)
- Comments (to indicate a treatment or any relevant information – optional)
- Center name, study phase and comments are not mandatory, but they will be reported in the output file and can be used to sort data in this file.

- X-calibration slope and offset. This information is necessary if output data from several devices have to be compared. X-calibration parameters will allow standardization of the TBS output values.

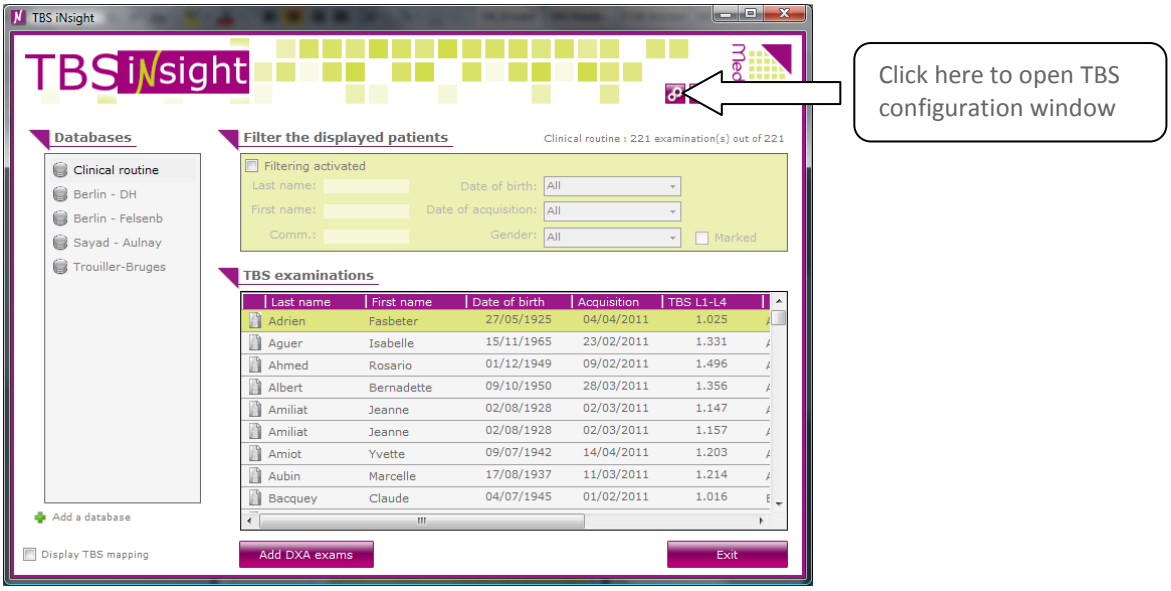
If DXA scans are not all in the same folder, check the "Include subdirectories" checkbox so that all scans contained in the selected directory and in all its subdirectories are taken into consideration.

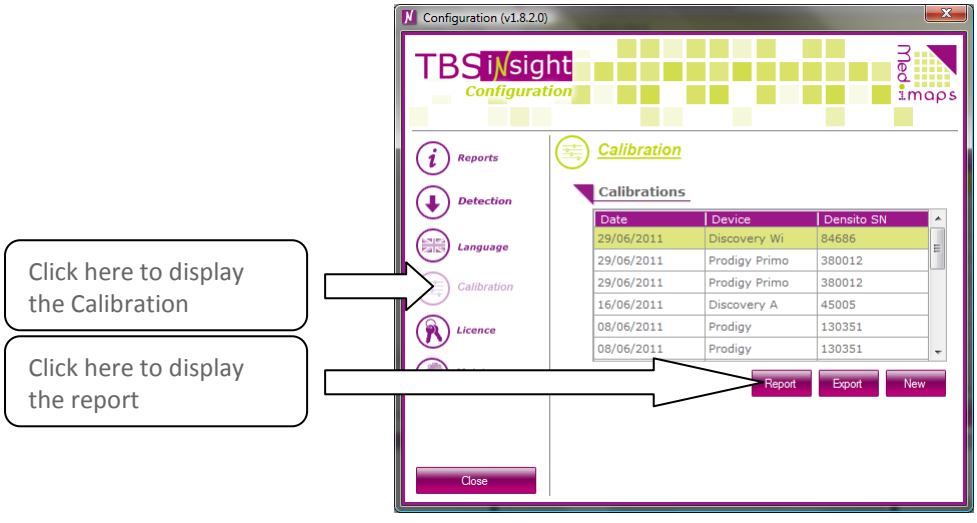
2. How to retrieve X-calibration parameters?

The process to obtain X-calibration parameters is different whether you own TBS iNsight software or not.

a. Users who own TBS iNsight Software

X-calibration parameters can be read in the TBS iNsight software:





The calibration report will be displayed and contains the X-calibration equation parameters:

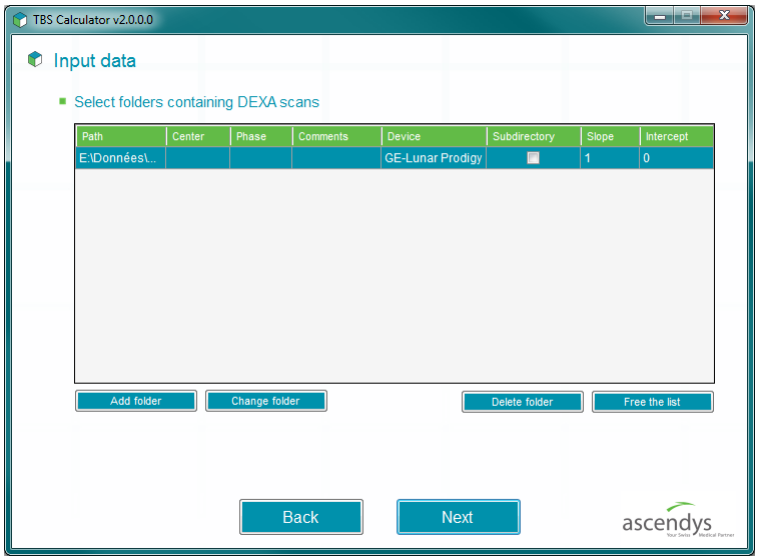
b. Users who do not own TBS iNsight Software

For users who do not own TBS iNsight software, the X-calibration parameters can be:

- Obtained by scanning a TBS phantom and sending scans to Med-Imaps for processing;
- Calculated from a large number of scans (analysis of the shift and / or drift of TBS values of the center as compared to normal population);
- Left to default values (since X-calibration parameters are usually close to 1 (slope) and 0 (offset).

3. List of folders

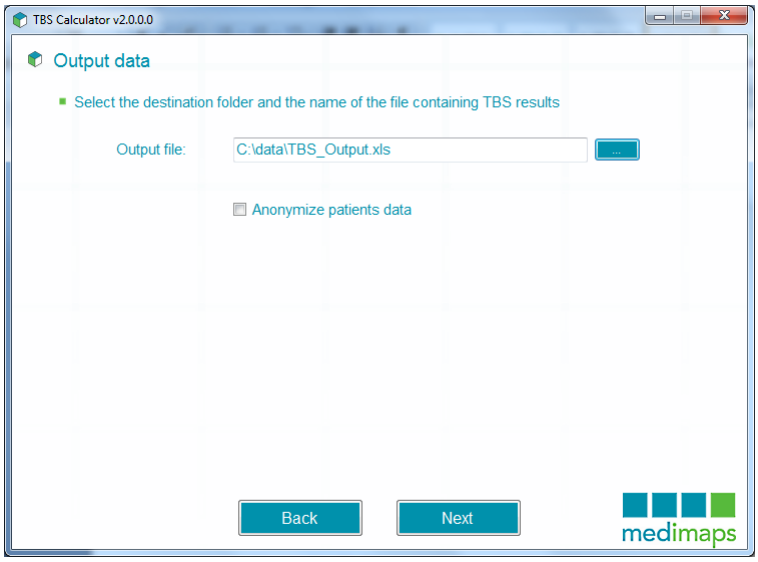
One can enter as many folders as necessary: one for each scanner, or one for each group of patients...



The input data folders can be modified or deleted using the corresponding buttons.

D. Output data

The results will be stored in a file. The user must indicate where to store it:



Depending on the output file format, one Excel file with 2 sheets or two CSV files will be created for each analysis: one containing the files that have been analyzed and one containing the rejected files. Some files will be rejected since:

- They are not DXA files;
- They do not contain a spine exam;
- BMD analysis has not been performed;
- They have been acquired on a scanner which serial number is not in the authorized list.
- They are encrypted (enCORE files);
- The TBS Calculator software cannot read them.

The output data will be anonymized, which means that the first and last names of the patients will be replaced by the word "REMOVED".

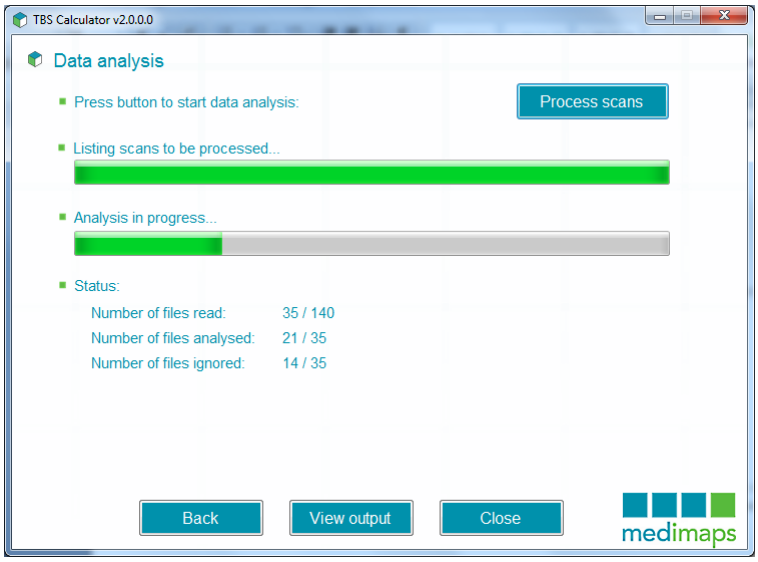
E. Files processing

There are 3 steps at this stage:

- Building the list of files to be analyzed;
- Checking if files can be analyzed;
- Calculating TBS.

In the data analysis window, a progress bar will indicate the number of scans analyzed and those still to be processed.

The “Abort analysis” button may be pressed at any time in order to abort analysis.



F. Results delivery

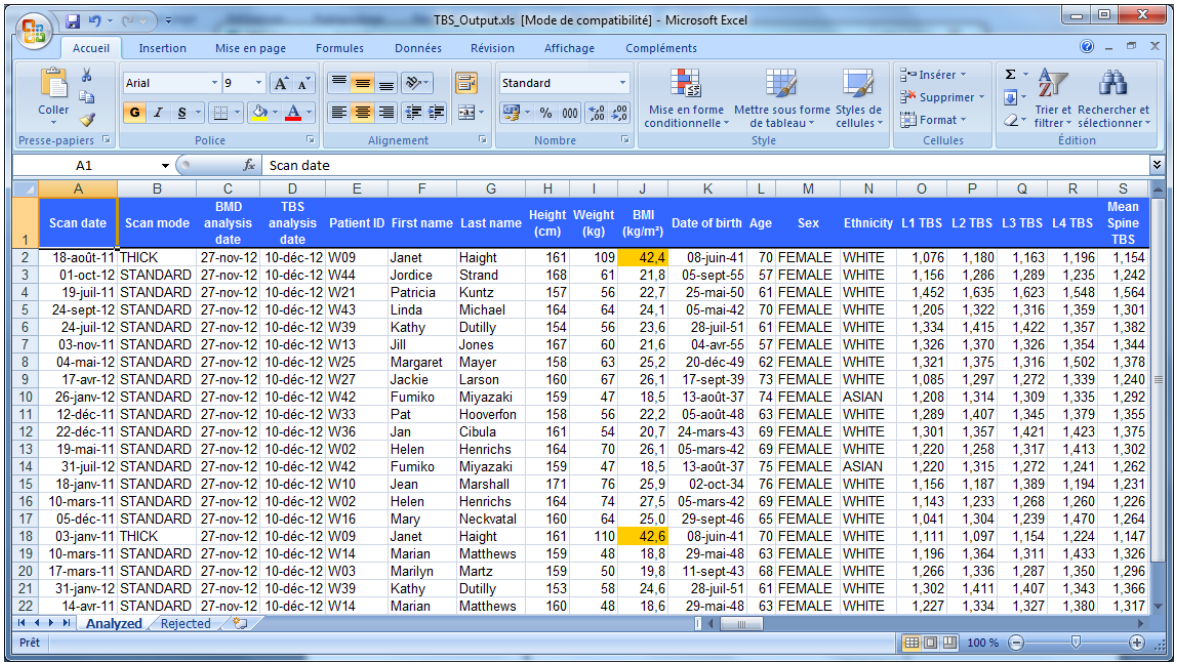
Once analyzed, the results will be made available to the user after a final check of the number of available scans analyzes of the corresponding license or study.

Users whose number of scans analyzes is limited will have to confirm that they accept to be debited of the corresponding number of scans before to be able to view the results.

G. View output file

Output file is a Microsoft Excel compatible file. The “View output button” allows opening that file in Microsoft Excel application, provided it is installed on the PC that runs this software. Otherwise, any spreadsheet and even text editors can open this file.

NB: if the output file is XLS formatted, unexpected values and values beyond accepted range are outlined using a specific color. For example, BMI values over 35 appear in an orange cell and values over 60 appear in a red cell. TBS values under 0 or over 2.0 appear also in red cells.



TBS_Output.xls [Mode de compatibilité] - Microsoft Excel

	Scan date	Scan mode	BMD analysis date	TBS analysis date	Patient ID	First name	Last name	Height (cm)	Weight (kg)	BMI (kg/m²)	Date of birth	Age	Sex	Ethnicity	L1 TBS	L2 TBS	L3 TBS	L4 TBS	Mean Spine TBS
2	18-août-11	THICK	27-nov-12	10-déc-12	W09	Janet	Haight	161	109	42,4	08-juin-41	70	FEMALE	WHITE	1,076	1,180	1,163	1,196	1,154
3	01-oct-12	STANDARD	27-nov-12	10-déc-12	W44	Jordice	Strand	168	61	21,8	05-sept-55	57	FEMALE	WHITE	1,156	1,286	1,289	1,235	1,242
4	19-juil-11	STANDARD	27-nov-12	10-déc-12	W21	Patricia	Kuntz	157	56	22,7	25-mai-50	61	FEMALE	WHITE	1,452	1,635	1,623	1,548	1,564
5	24-sept-12	STANDARD	27-nov-12	10-déc-12	W43	Linda	Michael	164	64	24,1	05-mai-42	70	FEMALE	WHITE	1,205	1,322	1,316	1,359	1,301
6	24-juil-12	STANDARD	27-nov-12	10-déc-12	W39	Kathy	Dutilly	154	56	23,6	28-juil-51	61	FEMALE	WHITE	1,334	1,415	1,422	1,357	1,382
7	03-nov-11	STANDARD	27-nov-12	10-déc-12	W13	Jill	Jones	167	60	21,6	04-avr-55	57	FEMALE	WHITE	1,326	1,370	1,326	1,354	1,344
8	04-mai-12	STANDARD	27-nov-12	10-déc-12	W25	Margaret	Mayer	158	63	25,2	20-déc-49	62	FEMALE	WHITE	1,321	1,375	1,316	1,502	1,378
9	17-avr-12	STANDARD	27-nov-12	10-déc-12	W27	Jackie	Larson	160	67	26,1	17-sept-39	73	FEMALE	WHITE	1,085	1,297	1,272	1,339	1,240
10	26-janv-12	STANDARD	27-nov-12	10-déc-12	W42	Fumiko	Miyazaki	159	47	18,5	13-août-37	74	FEMALE	ASIAN	1,208	1,314	1,309	1,335	1,292
11	12-déc-11	STANDARD	27-nov-12	10-déc-12	W33	Pat	Hooverfon	158	56	22,2	05-août-48	63	FEMALE	WHITE	1,289	1,407	1,345	1,379	1,355
12	22-déc-11	STANDARD	27-nov-12	10-déc-12	W36	Jan	Cibula	161	54	20,7	24-mars-43	69	FEMALE	WHITE	1,301	1,357	1,421	1,423	1,375
13	19-mai-11	STANDARD	27-nov-12	10-déc-12	W02	Helen	Henrichs	164	70	26,1	05-mars-42	69	FEMALE	WHITE	1,220	1,258	1,317	1,413	1,302
14	31-juil-12	STANDARD	27-nov-12	10-déc-12	W42	Fumiko	Miyazaki	159	47	18,5	13-août-37	75	FEMALE	ASIAN	1,220	1,315	1,272	1,241	1,262
15	18-janv-11	STANDARD	27-nov-12	10-déc-12	W10	Jean	Marshall	171	76	25,9	02-oct-34	76	FEMALE	WHITE	1,156	1,187	1,389	1,194	1,231
16	10-mars-11	STANDARD	27-nov-12	10-déc-12	W02	Helen	Henrichs	164	74	27,5	05-mars-42	69	FEMALE	WHITE	1,143	1,233	1,268	1,260	1,226
17	05-déc-11	STANDARD	27-nov-12	10-déc-12	W16	Mary	Neckvatal	160	64	25,0	29-sept-46	65	FEMALE	WHITE	1,041	1,304	1,239	1,470	1,264
18	03-janv-11	THICK	27-nov-12	10-déc-12	W09	Janet	Haight	161	110	42,6	08-juin-41	70	FEMALE	WHITE	1,111	1,097	1,154	1,224	1,147
19	10-mars-11	STANDARD	27-nov-12	10-déc-12	W14	Marian	Matthews	159	48	18,8	29-mai-48	63	FEMALE	WHITE	1,196	1,364	1,311	1,433	1,326
20	17-mars-11	STANDARD	27-nov-12	10-déc-12	W03	Marilyn	Martz	159	50	19,8	11-sept-43	68	FEMALE	WHITE	1,266	1,336	1,287	1,350	1,296
21	31-janv-12	STANDARD	27-nov-12	10-déc-12	W39	Kathy	Dutilly	153	58	24,6	28-juil-51	61	FEMALE	WHITE	1,302	1,411	1,407	1,343	1,366
22	14-avr-11	STANDARD	27-nov-12	10-déc-12	W14	Marian	Matthews	160	48	18,6	29-mai-48	63	FEMALE	WHITE	1,227	1,334	1,327	1,380	1,317

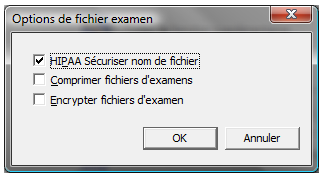
TBS Calculator output file, XLS formatted: Analyzed scans

H. Troubleshooting

Some files contained in the input folders may have been rejected during the files processing. The reasons may be:

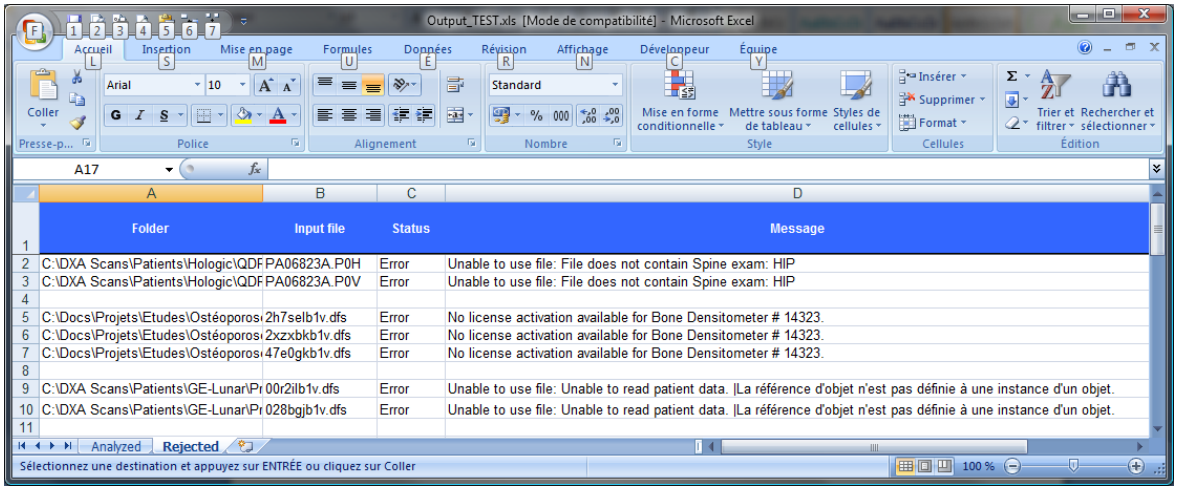
- The file contain no Spine exam
  - Select only scan files with a spine acquisition

- The file cannot be read by TBS Calculator, because it has been crypted and or compressed by enCORE software. If so, a message indicating **"Unable to use file: Unable to read patient data. |Object reference is not set to an instance of an object"** will be displayed in the rejected files sheet (if .xls formatted) or file (if .csv formatted).
  - Open enCORE software and
    - Untick the Compression and Encryption options (User Options > Systems > Exam files Options)



    - Re-analyze the scans.

- The file has been acquired by a DXA scanner that is not included in the scanners listed in the license.
  - Select only scan files acquired by DXA scanners for which you have a license or contact your retailer to get an extension of your license with additional scanners.



TBS Calculator output file, XLS formatted: Rejected scans

MED-IMAPS
TECHNOLOGICAL PLATFORM FOR BIOMEDICAL INNOVATION
HOPITAL XAVIER ARNOZAN
AVENUE DU HAUT-LEVEQUE
33600 PESSAC
FRANCE
Phone: +33 557 102 856

After-sales service:
Email: support@tbsinsight.fr
Tel: +33 557 102 872

III. Appendices

A. Revisions history

Revision	Date	Author(s)	Comment	Status
2.0	07 Dec 2012	Christophe LELONG	First version, which is an update of the TBS - Clinical Data Analyzer User guide, v1.8	

B. Validations history

Revision	Date	Author(s)	Comment
2.0	12 Dec 2012	Christophe LELONG	OK