EXILIS Device,
Effect on Porcine Fat Tissue

FINAL REPORT

Non-GLP Study

Copy	1 of 3
Identification No.:	553/08
Study initiation date:	December 24, 2008
Final Report date:	April 30, 2009

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COMPLIANCE STATEMENT

I, the undersigned hereby declare that the objectives laid down in the report were achieved and as no untoward incidence occurred to adversely affect the quality or integrity of the study, I consider the data generated to be valid. This report fully and accurately reflects the procedures used and data generated in the course of this study.

Name of the Study: **EXILIS Device, Effect on Porcine Fat Tissue**

Identification No.: 553/08

Name of the Test Device: EXILIS

Study initiation date: December 24, 2008

Date of Final Report: April 30, 2009

Date: 30.4. 2009

Signature: .....

Lukáš Pánek, MVDr.
Study director

SUMMARY

The purpose of this study was to prove the health safety of the combination of radiofrequency and ultrasound energies generated by the EXILIS Device on the pig, to find out the warming up effectiveness of the said combination on skin and subcutaneous fat tissue of the pigs, to assess the effect of the radiofrequency and its combination with the ultrasound on the skin and subcutaneous fat tissue of the tested animals.

The study was conducted using 3 pigs (3 females). Two of them were domestic pigs (P1, P2) and the third was Vietnamese pig (V3). The animals were divided into groups: Group 1 and Group 2. Animals P2 and V3 were in Group 1 and animal P1 was in Group 2. Each animal received an appropriate treatment using the EXILIS Device on marked areas (20 × 10 cm) by radiofrequency at the power output in the range of 90-120 W and the ultrasound with preset power output 3W/cm^2 for 10-25 minutes.
The animals from Group 1 went through this one treatment using the EXILIS Device. The animal from Group 2 went through six such treatments. After the treatment, the animals from Group 1 were sacrificed and the animal from Group 2 spent two weeks of recovery period and then was sacrificed.

Temperature of the subcutaneous fat tissue was measured in all the animals during each treatment by means of an internal probe with 4 thermo-sensors in the whole vertical column of the fat tissue. The superficial temperature was measured, too, by means of an external EXILIS thermometer.

Clinical signs and mortality were recorded daily in all the animals during acclimation and continuously during treatment and recovery periods.

Blood samples for biochemical evaluation were collected from animal P1 (Group 2) before the first, after the third, fifth and sixth treatment, and at the end of the recovery period.

The skin with subcutaneous fat tissue biopsy samples for histopathological evaluation were taken from animals P2 and V3 (Group 1) before (control biopsy) and after the single treatment using the EXILIS Device. The biopsy samples from animal P1 (Group 2) were taken before (control biopsy) and after the 1st treatment, after the 2nd, 4th, 5th, 6th treatment, and at the end of the recovery period from both areas. Also samples of the lungs and liver were taken for histopathological evaluation from animal P1 at the end of the recovery period. The histopathological evaluation was mainly focused on the pathological changes in subcutaneous fat tissue such as necrosis of the adipocytes, extensive disintegration of fibrous tissue and further changes, such as apoptosis, neocapilarisation, and neovascularisation of fat tissue, hyperaemia of fat tissue, defibrotisation and local immune response. The histopathological evaluation of the lung samples was focused on signs of embolisation and that of the liver samples was focused on signs of steatosis.

RESULTS

Both animals from Group 1 very well tolerated the single treatment by means of the EXILIS Device: no signs of toxicity were recorded. No clinical changes of the skin at the site of the treatment were observed.
Similarly, animal P1 from Group 2 very well tolerated all the treatments performed by means of the EXILIS Device. The skin was without any clinical signs of toxicity in the treated area. During the recovery period, no clinical signs of toxicity were observed.
The temperature of the treated area reached the planned treatment level in the range of 39-43°C, and was kept for at least 2-3 min. The temperature gradient in the treated area was measured with the peak temperature achieved in the depth of targeted fat tissue.

Biochemistry examination of animal P1 from Group 2 did not reveal any considerable changes of the bilirubin, total cholesterol, HDL, LDL and triglycerides levels. Only an increase in the ALT and AST levels (within physiological limits) was found during the treatment period without relation to the treatment.

The histopathology examination of the skin and subcutaneous fat tissue from both animals of Group 1 after the single treatment by means of the EXILIS Device did not reveal any pathological changes caused by this treatment.

Animal P1 from Group 2 was separately treated six times using the EXILIS Device. The histopathological examinations of the skin samples taken in the intervals mentioned did not show any pathological changes caused by this type of repeated treatment. Focal pneumonia, most probably of mycoplasm origin, was found in lungs of this pig, but it was not caused by the EXILIS-Device treatment. No signs of embolisation were found in the lungs. Marked venostasis was observed in all the liver lobes, and Oil red O staining did not show any presence of lipid substances in the liver parenchyma.
The histopathology examination of the skin and subcatenous fat tissue from animal P1 taken in the intervals mentioned showed evidence of neocapilarisation and neovascularisation of the fat tissue, hyperaemia of fat tissue, defibrotisation and local immune response. For details see the Appendix.

CONCLUSION

The EXILIS treatment was clinically well tolerated both after the single application and after the six treatments as well. This therapy, i.e. the combination of the radiofrequency waves in the dose of 90-120 W with the ultrasound energy in the dose of 3W/cm^2 for 10-30 minutes did not cause any pathological changes during the six treatments and after them.

Biochemistry examination did not find any treatment-related changes of the parameters monitored in the pig that was six times treated by means of the EXILIS Device.

The EXILIS Device as a source of the radiofrequency and ultrasound energies is safe in the doses used in this study and did not cause any clinical or biochemistry changes. The EXILIS Device proved the effectiveness of the warming up of the subcutaneous fat tissue of the pigs.
The histopathology examination of the fat tissue found treatment-related changes in the tissue during the six treatments and after them.

ABBREVIATIONS

P1	Domestic pig, Group 2, six treatments and recovery
P2	Domestic pig, Group 1, one treatment
V3	Vietnamese pig, Group 1, one treatment
RČH	Registration number of the breeding farm
Rpm	Round per minute
HDL	High density lipoproteins
LDL	Low density lipoproteins
AST	Aspartate animotransferase
ALT	Alanine aminotransferase
CHOL	Cholesterol
Bili	Bilirubin total
TAG	Triglycerides

1. INTRODUCTION

1.1. Aim of the Testing

The purpose of this study was to prove the health safety of the combination of radiofrequency and ultrasound energy generated by the EXILIS Device on the tested animals, to find out the effectiveness of the said combination on fat tissue of the pigs, to assess the effect of the radiofrequency and its combination with the ultrasound on the fat tissue of the tested animals, and to measure the temperature in the subcutaneous fat tissue.

1.2. Guidelines

This laboratory study which is designed as a non-GLP study was carried out according to relevant SOPs of BioTest s.r.o..

1.3. Facility Management and Animal Husbandry

Animal care was in compliance with the SOPs of BioTest s.r.o., the European convention for the protection of vertebrate animals used for experimental and other scientific purposes (ETS 123), the Act of the Czech National Assembly, Collection of laws No. 246/1992, inclusive of the amendments, on the Protection of animals against cruelty, and Public Notice of the Ministry of Agriculture of the Czech Republic, Collection of laws No. 207/2004, as amended, on keeping and exploitation of experimental animals. BioTest s.r.o. is a holder of the Accreditation Certificate for users issued by Central Committee for Animal Protection of the Czech Republic in compliance with the Act of the Czech National Assembly.

1.4. Animal Welfare Act Compliance

The study was prepared for this type of experiment and approved by the Institutional Animal Care and Use Committee (IACUC) and the Committee for Animal Protection of the Ministry of Industry and Trade of the Czech Republic (138/2008). Procedures used in this study were designed to conform to accepted practices and to minimize or avoid causing pain, distress, or discomfort to the animals. The number of animals selected for use in this study was considered to be the minimum number necessary to meet scientific value for this type of study.

2. TEST CONDITIONS

2.1. Description of the Test Device

Name of the Test Device:	EXILIS
Producer:	BTL Industries Limited 161 Cleveland Way Stevenge SG1 6BU Hertfordshire United Kingdom
Power output (max.): radiofrequency ultrasound	 120 W 3 W/cm^2
Frequency:	2 MHz

Name of the Internal Probe:	Physitemp IT-17/4B
Producer:	SCIENCE PRODUCTS GmbH D-65719 Hofheim
Description:	Flexible bending teflon probe with 4 thermo sensors in 1 centimeter distance among them.
Accuracy:	0.1°C
Range:	0-50°C

Name of the Temperature Data Logger:	PICO TC-08
Producer:	Pico Technology James House PE19 84D Cambridgeshire United Kingdom
Accuracy:	0.5°C

Treatment principle:

The treatment device is working on the basis of simultaneous combination of radiofrequency and ultrasound. The radiofrequency has a deep thermal effect and the ultrasound is working on the basis of the acoustic wave with insignificant thermal effect.
The exposure time of the treatment device on skin and fat tissue was 10-25 minutes till warming up the treated area to the temperature of 39-43°C. The exposure time depended on surrounding temperature, and it was prolonged if the surrounding temperature was lower. This exposure time also depended on anesthesia. The tissue temperature was measured in the designated areas *via* internal probe in the whole vertical column of the fat tissue. The superficial temperature was measured, too, using an external EXILIS thermometer.
The temperature gradients are attached as an Appendix of this Study.

2.2. Experimental Design

Procedure:	**Date:**
Study Initiation Date:	December 24, 2008
Animal Receipt:	December 24, 2008
Acclimation:	7 Days
Start of Experimental Part:	December 24, 2008
First Procedure:	December 30, 2008
End of the Experimental Part:	March 17, 2009
Study Completion Date (Final Report):	April 30, 2009

A synopsis of the animal experiment:

Group 1: animals P2 and V3

Procedure:	**Timing:**
Treatment frequency:	Once
Anaesthesia:	during treatment and biopsy
Biopsy:	before treatment and after treatment

Group 2: animal P1

Procedure:	**Timing:**
Treatment frequency:	1 per week (the total number 6)
Exposure time:	10-25 minutes till warm up the tissue around 39-43°C
Anaesthesia:	during each treatment, biopsy and blood sampling
Blood sampling:	before treatment, after the 3rd treatment, after 5th treatment, after the last treatment and 2 weeks follow up the end of the treatment
Biopsy:	before treatment, after the first treatment, after 2nd, 4th,5th, 6th treatment and 2 weeks follow up the end of the treatment (recovery period)
Histological sample of liver and lung:	after the end of the recovery period
Recovery period:	2 weeks

2.3. Test System

Species & Strain:	2 domestic pigs and 1 vietnamese pig
Supplier:	Zemědělské obchodní družstvo Zálabí Na Františku 358 Ovčáry 280 02 RČH 21012961 The vietnamese pig was bought from private farmer without RČH
Age at delivery: domestic pigs Vietnamese pig	 6-8 months 4 years
Total number of animals: Group 1: Group 2:	3 1 domestic pig and 1 vietnamese pig 1 domestic pig
Animal identification:	Individual ear mark

2.4. Animal Selection, Randomization & Group Assignment

The animals were divided into the two group according sponsor's request.

2.5. Justification of the Test System

Pigs are suitable animal model for testing of the skin reaction due to its similarity to human skin.

2.6. Housing

The study animals were individually housed in pens, environmentally monitored and ventilated rooms maintained at a temperature of 10-24°C. Cleaning of pen and surrounding area was performed on daily basis. Food and water containers were changed and sanitized twice weekly.

2.7. Diet
During the acclimation and study periods the animals were fed with complete cereal diet for pigs (CDP, ZZN Polabí, a.s., Czech Rep.), in amount of 25 g kilogram of the body weight for animal per day.

2.8. Water
Water of monitored quality was supplied *ad libitum* (free access to water) during the acclimation and study periods. There were no contaminants in the water at levels that could reasonably be expected to affect the purpose or integrity of the study. Copies of the analyses are kept in the archive of BioTest s.r.o.

2.9. Acclimation
The animals were acclimated for 7 days. No prophylactic or therapeutic treatment was administered during the acclimation or study periods. Only animals in good health conditions were used for the study.

2.10. Animal Identification
Each tested animal was individually identified by ear mark.

3. METHODS

3.1. Treatment Procedure

Group 1: animals P2 and V3

One area (20 × 10 cm) of the skin in *regio abdominalis*, without any visible changes, was selected in the both animals and labelled by a marker.

Course of the treatment

Animal No.	one treatment	
	min	W
P2	15	100
V3	20	100

Group 2: animal P1

One area (20 × 10 cm) of the skin was selected on the experimental animal in *regio abdominalis*, without any visible changes and labelled by a marker.

Course of the treatment

Animal No.	1st treatment		2nd treatment		3rd treatment		4th treatment		5th treatment		6th treatment	
	min	W	min	W	min	W	min	W	min	W	min	W
P1	25	90-120	20	100-120	22	100-120	25	110-115	20	115	24	115-120

During each treatment and biopsy, the animals were in total anesthesia under supervision of the veterinarian according to paragraph 3.2.

3.2. Anaesthesia

Type:	Dose: (mg/kg)	Administration:
Diazepamum	1	i.m.
Azaperonum	8	i.m.
Ketamine	5	i.m.
Propofolum	2	i.v.

3.3. Temperature Measuring

After achieving the external skin surface temperature of 38°-40 °C, which was measured by means of the EXILIS Device, the internal probe was inserted at the angle of 25° into the whole column of the subcutaneous fat tissue. The superficial temperature was measured by means of the external EXILIS thermometer as well. The treatment temperature was kept for at least 2-3 minutes.

3.4. Clinical Signs and Mortality

Daily Observations: All pigs were observed for clinical signs, morbidity or mortality once a day in acclimation and during treatment period.

Clinical Observations included: Signs of toxicity, changes in the skin, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous system, somatomotoric activity and behavior pattern, changes in gait, posture and response to handling, the presence of clonic or tonic movements and stereotypes.

3.5. Clinical Pathology

Blood Analyses:
Blood samples for clinical chemistry were collected from Group 2 animal (P1), before the first treatment, after the 3rd treatment, after the 5th treatment, after the last one and two weeks after the end of the treatment (recovery period). Blood was taken by venepuncture of *v. auricularis intermedia* under total anesthesia (see 3.2). Blood samples were collected into tubes Tapval without anticoagulation (clinical chemistry), serum samples were obtained by centrifugation at 6000 rpm for 15 minutes. Serum for clinical chemistry (ca 1 ml) was transferred into appropriately labelled and sealed Eppendorf tubes and frozen at -20º C or below until transport to analyses (SOP-HEM, SOP-BCH).
Test Facility (Laboratory of Hematology and Biochemistry) was responsible for sample preparation and transport of serum samples to the Test site. The Test site (Clinical Biochemistry Dept. of Hospital Pardubice) was responsible for determination of biochemical parameters of serum samples by DIMENSION RxL MAX. Raw data results were delivered to BioTest Laboratory of Hematology and Biochemistry. Results evaluation, reporting and archiving of Test Site raw data were performed by Test Facility (Laboratory of Hematology and Biochemistry).

Clinical Chemistry: Following parameters were determined:

Cholesterol (Chol)	Dimension RxL MAX Siemens, Siemens CHOL	mmol/l
HDL Cholesterol	Dimension RxL MAX Siemens, Siemens AHDL	mmol/l
LDL Cholesterol	Roche Cobas Integra 400, Cobas LDL C	mmol/l
Alanine amino transferase (ALT)	Dimension RxL MAX Siemens, Siemens ALT	µkat/l
Aspartate amino transferase (AST)	Dimension RxL MAX Siemens, Siemens AST	µkat/l
Bilirubin total (Bili)	Dimension RxL MAX Siemens, Siemens TBIL	µmol/l
Triglycerides (TAG)	Dimension RxL MAX Siemens, Siemens TGL	mmol/l

3.6. Pathology Procedures

Histological examination:
The biopsy samples of the skin and subcutaneous fat tissue were taken from designated areas *via* needle biopsy before (control biopsy) and after one treatment from both animals of Group 1 (P2, V3). The biopsy samples from Group 2 animal (P1) were taken the in same way before the treatment (control biopsy), after the first treatment from area A, after the 2^{nd}, 4^{th},5^{th}, 6^{th} treatment, and 2 weeks after the end of the treatment (recovery period) from both areas. The samples from three main liver lobes and from lungs were also taken from this animal for histopathological examination at the end of the recovery period.

Fixation

The biopsy skin samples together with the liver and the lung samples were fixed in 4 % neutral buffered formaldehyde.

Histology

Histological slides were made by common paraffin technique and stained with haematoxylin and erythrosin (HE). Frozen sections from three liver lobes of pig P1 were stained with Oil red O for the presence of lipid substances. (SOP PAT).
The histopathological evaluation was focused mainly on the pathological changes in fat tissue such as necrosis of the adipocytes, extensive disintegration of fibrous tissue and further changes, such as apoptosis, neocapilarisation and neovascularisation of fat tissue, hyperaemia of fat tissue, defibrotisation and local immune response.
The histopathological evaluation of the lung samples was focused on signs of embolisation and that of the liver samples was focused on signs of steatosis.

4. RESULTS

4.1. Clinical Signs and Mortality

All the animals were in good health condition throughout the acclimation period.
Both the animals from Group 1 very well tolerated the single treatment by means of the EXILIS Device, and no signs of toxicity were recorded. No clinical changes of the skin at the site of the treatment were observed.
Similarly, pig P1 from Group 2 very well tolerated all the treatments performed by means of

the EXILIS Device. The skin at the site of both treatments exhibited no clinical signs of toxicity. During the recovery period no clinical signs were observed in this pig.

4.2. Temperature Measuring

The temperature of each treatment in all the animals reached the intended level in the range of 39-43 °C and was kept for 2-3 minutes. After the end of treatment the temperature quickly decreased. The temperature gradients are attached as an Appendix of this Study (Fig. 8 and 9).

4.3. Clinical Chemistry Evaluation

Individual values of the parameters determined are presented in Table 1.

The values of Bilirubin varied minimally (5 to 7 umol/l) during the whole study and recovery period.
The values of Total cholesterol (1.61-1.93 mmol/l), HDL (0.50-0.70 mmol/l) and LDL (0.85-1.26 mmol/l) cholesterols and Triglycerides (0.2-0.5 mmol/l) slightly varied within the physiological limits without any considerable differences in all five examinations.
An increase in the Alanine amino transferase serum activity was observed in Examination 2 (by 51 %) and in Examination 3 (by 88 %) as compared to Examination 1. These values mildly decreased in Examination 4 and 5 when compared to Examination 3.
Very similar situation was recorded in the Aspartate amino transferase serum activity, where the individual values of AST increased by 57 % in Examination 3 and by 98 % in Examination 5 as compared with Examination 1.
The mentioned changes of both the parameters (ALT and AST) were within the physiological ranges, which are 0.5-1.0 µkat/l and 0.5-1.5 µkat/l for ALT and AST, respectively, so they were biologically insignificant and without relation to the treatment.

Table 1: Clinical chemistry – Individual animal values

Animal No.:	Examination No.:	Date	Bilirubin µmol/l	ALT µkat/l	AST µkat/l	Chol mmol/l	HDL mmol/l	LDL mmol/l	TAG mmol/l
P1	1	23.01.2009	5	0.35	0.66	1.87	0.60	1.23	0.2
	2	30.01.2009	7	0.53	0.65	1.93	0.60	1.26	0.4
	3	16.02.2009	6	0.66	1.04	1.72	0.50	1.07	0.2
	4	02.03.2009	7	0.44	0.66	1.61	0.60	0.85	0.5
	5	17.03.2009	6	0.53	1.31	1.69	0.70	0.98	0.2

4.4. Histopathological Evaluation

Results and discussion

1. Group 1 (Animals P2 and V3)

Both these animals were once treated by means of the EXILIS Device. The histopathology examination did not reveal any pathological changes in the skin and subcutaneous fat tissue caused by the treatment.

2. Group 2 (Animal P1)

This pig was treated separately six times by means of the EXILIS Device. The histopathological examination of the skin samples taken in the above-mentioned intervals did not show any pathological changes caused by this type of treatment. Focal pneumonia, most probably of mycoplasm origin, was found in lungs of this pig. No signs of embolisation were found in lungs. Marked venostasis was observed in all the liver lobes, and Oil red O staining did not reveal the presence of lipid substances in the liver parenchyma.

Both in Group 1 animals and in Group 2 animal, the histopathological evaluation of the subcutaneous fat tissue did not reveal such changes as necrosis of the adipocytes and extensive disintegration of fibrous tissue. Following treatment-related changes were observed in the tissue during and after the six treatments: presence of deformed adipocytes, neocapilarisation and neovascularisation of fat tissue, disintegration of fibrous tissue, mild hyperplasia of mature collagen fibre, hyperaemia of fat tissue. For details see Appendix (Fig. 1-7).

5. CONCLUSIONS

The EXILIS treatment was clinically well tolerated both after the single application and after the six treatments as well. This therapy, i.e. the combination of the radiofrequency waves in the dose of 90-120 W with the ultrasound energy in the dose of 3W/cm^2 for 10-25 minutes did not cause any pathological changes after six treatments.

Biochemistry examination did not find any treatment-related changes of the parameters monitored in the pig that was six times treated by means of the EXILIS Device.

EXILIS treatment at the dose used did not cause any pathological changes in the skin and subcutaneous fat tissue during the six treatments and after them.

The EXILIS Device as a source of the radiofrequency and ultrasound energies is safe in the doses used in this study and did not cause any clinical or biochemistry changes. The EXILIS Device proved the effectiveness of the warming up of the subcutaneous fat tissue of the pigs.

The histopathology examination of the fat tissue found treatment-related changes in the tissue during the six treatments and after them.

APPENDIX

Histopathological Findings and Temperature Gradients

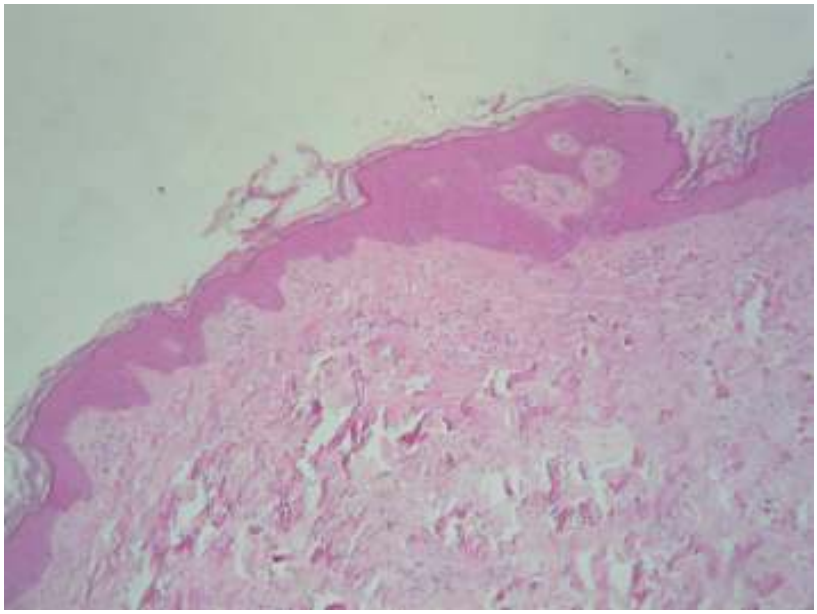

Fig. 1: Skin tissue before EXILIS treatment from the pig P1. Normal appearance.
(HE; objective 20)

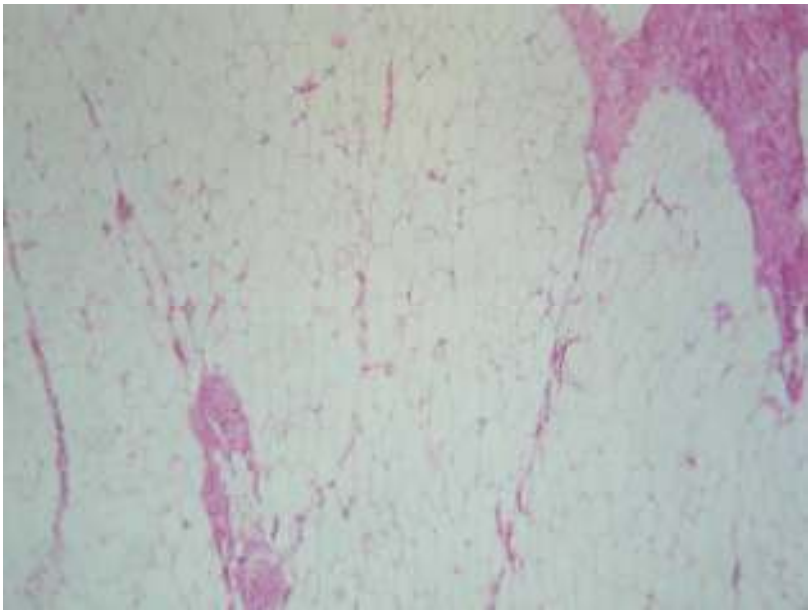

Fig. 2: Subcutaneous fat tissue before EXILIS treatment from the pig P1. Normal appearance.
(HE; objective 20)

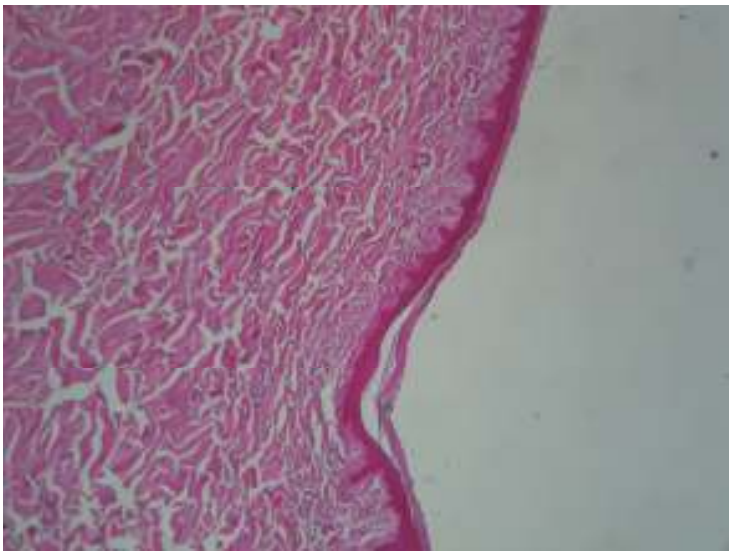

Fig. 3: Skin tissue after the 6th EXILIS treatment from the pig P1. No pathology changes in epidermis. Neovascularisation in the corium, presence of fibroblasts and histiocytes.
(HE; objective 20)

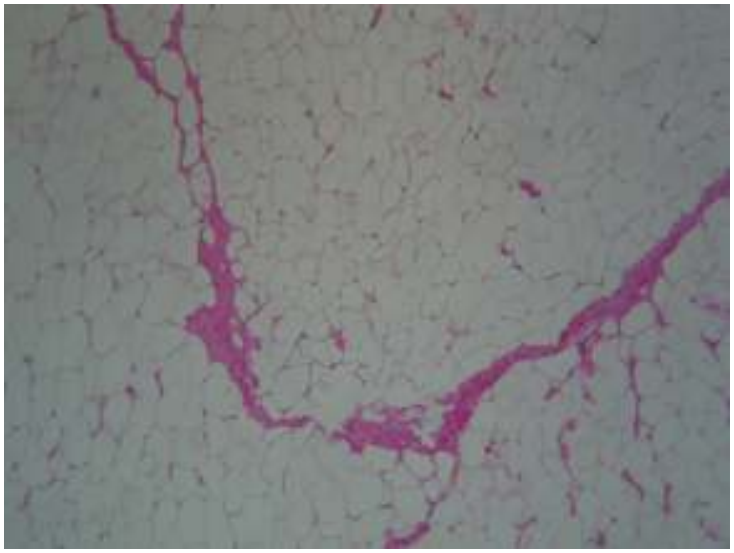

Fig. 4: Subcutaneous fat tissue after the 6th EXILIS treatment from the pig P1. No pathology changes. Presence of deformed adipocytes and granuloms, neocapilarisation and neovascularisation of fat tissue, disintegration of fibrous tissue, mild hyperplasia of mature collagen fibre, hyperaemia of fat tissue.

(HE; objective 20)

Defibrotisation of subcutaneous tissues. White adipose tissue is particularly concentrated in localized deposits located in the so-called lobulus (isolated clusters of individual adipocytes separated from one another by fibrotic septs). Metabolically it is virtually inaccessible. Typical effect of U.S. is a mechanical microvibration of treated tissue, with a consequent gradual disintegration of pathological incurred fibrous septs among lobulus and also among individual fixed adipocytes located in them. At a frequency of 2 MHz, there is a gradual metabolic accessing of fat tissue stock, with disintegration of mechanical linkages with the dermis.

Neovascularisation and neocapilarisation of fat tissue is a synergistic effect of US and high-frequency currents. In hypertrofic depots of white fat there is a relative loss of vascular bed – both arterial and venous. On the basis of new research we can not mark the white fat tissues simply as a passive body specified at the collection of energy stocks. This tissue is relatively dynamic – it produces and dislodges series of peptides and hormones into circulation. Relative devascularisation not only suppresses para and endocrine functions, but also significantly reduces oxygen supply to these tissues as well as its utilization and subsequent lipolytic processes as well. Neovascularisation is a long-term effect allowing gradual metabolisation of existing deposits of fat. The prevention of further deponation is significant. Lipolysis is the oxidative process, anaerobically the fat is non-metabolizable. Due to this effect, utilization of TGA occurs, vacuoles in the treated tissue become partially empty and thus the size of individual adipocytes is reduced.

Vasodilatation and hyperaemia. These effects allow a more accessible thermal effect on adipocytes (see temperature gradients), delivering run-off fat cells into the lymphatic channels, resulting in the progressive metabolization of fat deposits. One of the fundamental difficulties of these fat deposits is a local insulin resistance. Thanks to considerable hyperaemia, which persists in long-term even after the end of therapy, the ability of tissues to respond to insulin is increased, thus allowing higher metabolic (especially lipolytic) activity.

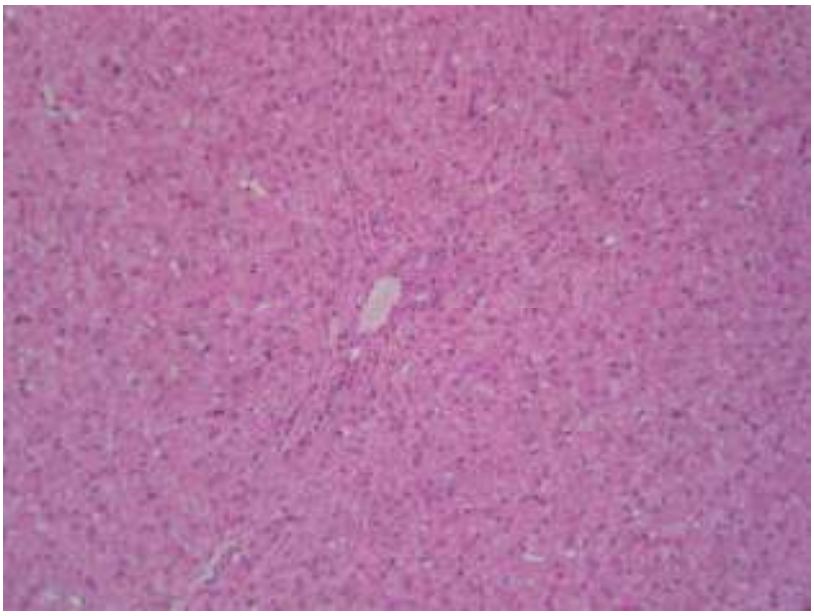

Fig. 5: Liver tissue at the end of study from the pig P1. No pathology changes.
(HE; objective 20)

Fig. 6: Liver tissue at the end of study from the pig P1. No presence of lipid substances.
(Oil red O; objective 20)

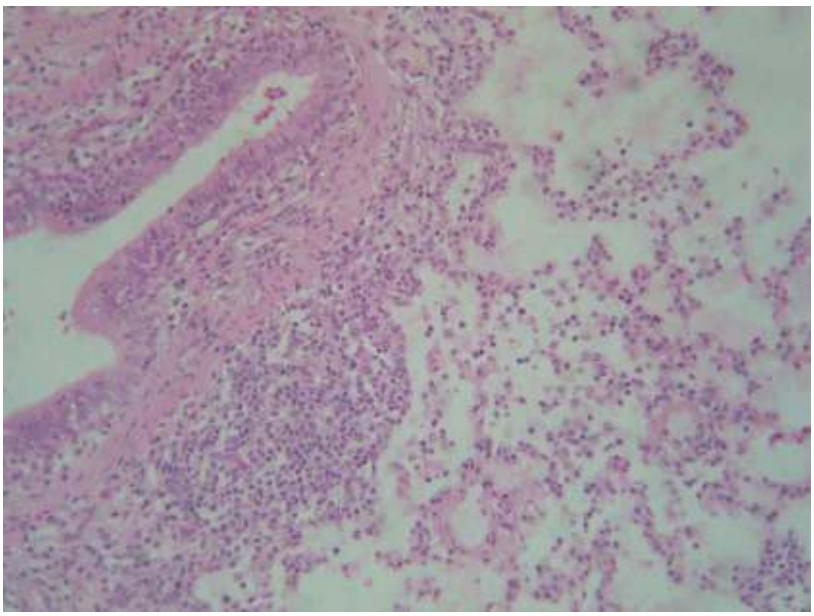

Fig. 7: Lung tissue at the end of study. Section from the lung of the pig P1 with mycoplasmal pneumonia. Shown are peribronchial lymphoid cell infiltration and macrophages and neutrophils in the alveoli.
(HE; objective 20)

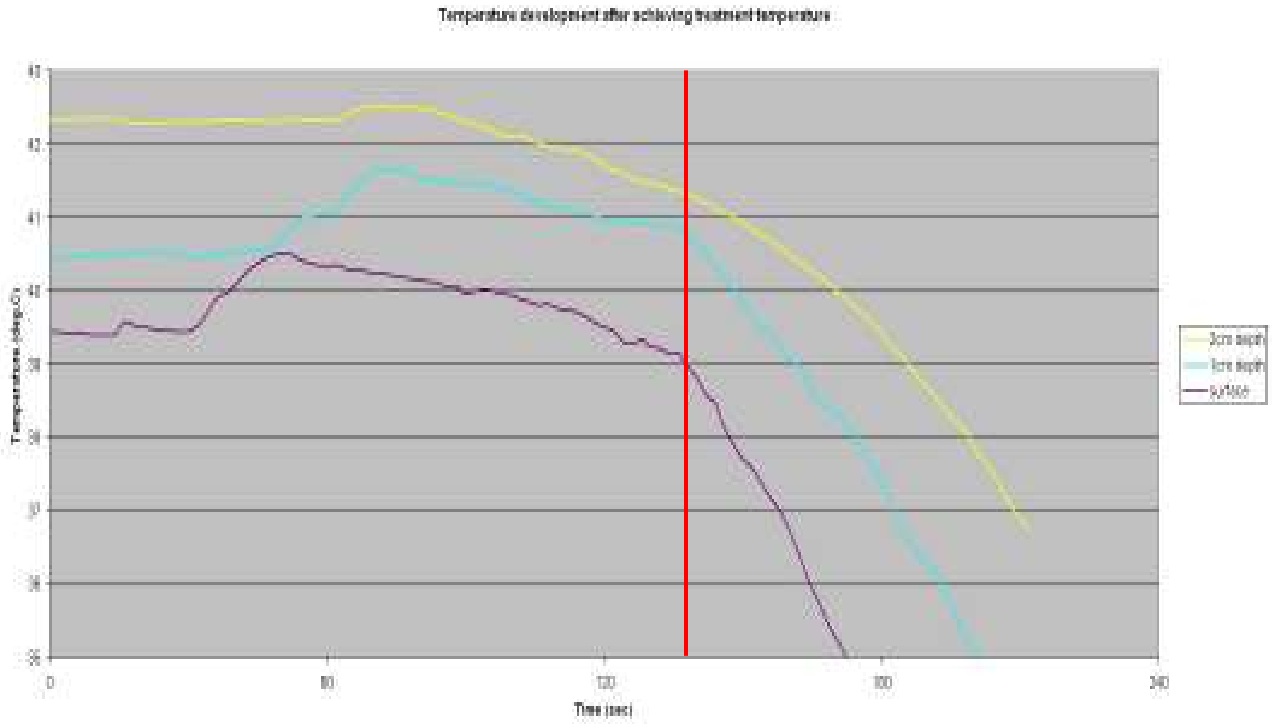

Fig. 8: Temperature gradients in the treated area of Animal P1 from the sixth EXILIS treatment. Changes are shown from an internal probe with thermo-sensors which took temperature measurements at different tissue depths during and after the EXILIS therapy. When the function for the cooling of the skin surface is active, it causes an increase in the difference in temperature between that on the surface and that at the depth of one-centimeter. This temperature difference changes from less than 0.15C° up to almost 2°C. The end of therapy is marked with a straight red line. At the end of the therapy, a significant drop in the tissue temperature can be seen at all depths.

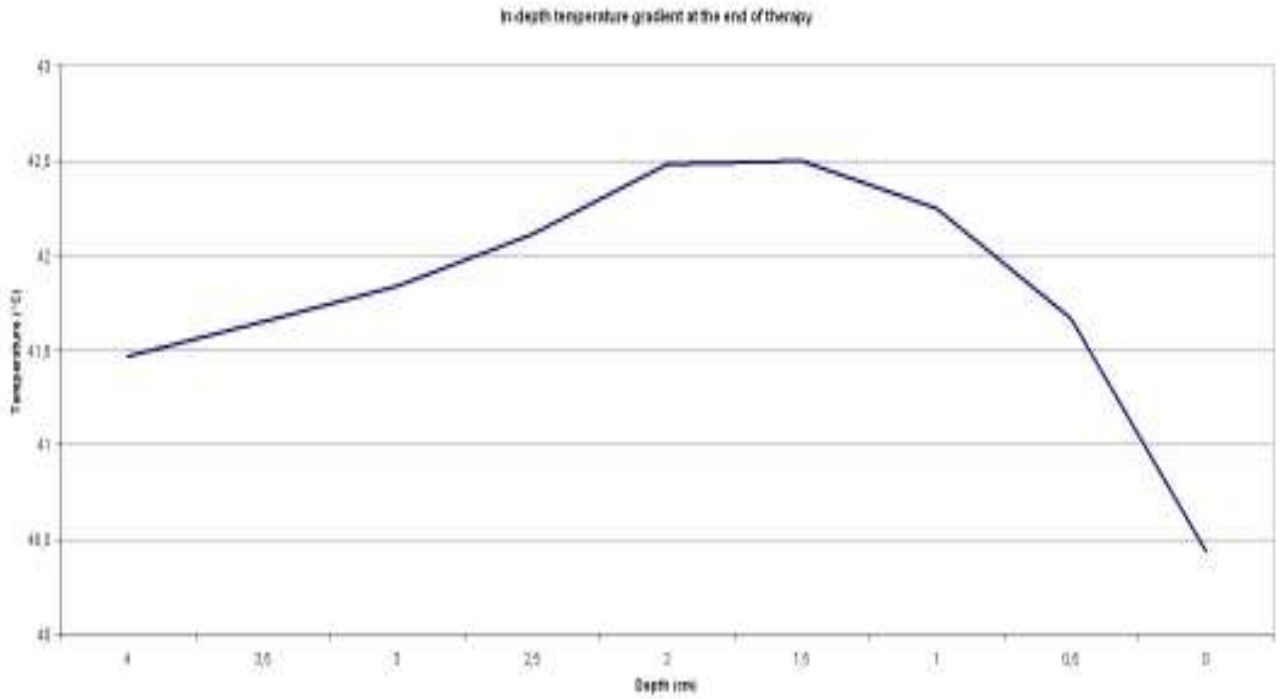

Fig. 9: Temperature gradients in the treated area of Animal P1 from the sixth EXILIS treatment. The chart above depicts the temperature measurements from internal probe with thermosensors at the end of an EXILIS therapy session. The probe was pulled from depth to the surface and the temperature was recorded at various depths. The resulting model characterizes the temperature gradient in the tissue. The highest temperature was measured at a depth of one to three centimeters below the surface, which corresponds to the depth of a targeted tissue. The difference between the surface temperature and the deep tissue temperature was 2°C.