

Radiologic and histological observations in experimental T1–T12 dorsal arthrodesis

A qualitative description of T1-T12 segment and other body parts involved, between prepubertal age and skeletal maturity

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ABSTRACT

Background: This experimental study provides a qualitative description and the morpho-structural features of the fusions taking place in the thoracic spine between prepubertal age and skeletal maturity. There is a lack of informations regarding the influence of partial or total dorso-thoracic vertebral arthrodesis on the development of the thoracic cage as well as its potential effects on different intra and extra-thoracic organs. This study admits the hypothesis that vertebral arthrodesis may have influence on other body areas and so, it intends to verify the possible secondary involvement of other body parts, such as intervertebral discs, cervical and thoracic spinal ganglia, sternocostal cartilage, ovaries and lungs.

Materials and Methods: Fifty-four female New Zealand white rabbits were submitted to dorsal arthrodesis. The radiologic imaging and light microscopy histological pictures were taken and studied in all. Computed tomography (CT) scan measurements were performed in operated and sham operated rabbits at different time. Similarly, histological specimens of intervertebral discs, cervical and thoracic spinal ganglia, sternocostal cartilage, ovaries and lungs were analyzed at different times. The study ended at the age of 17–18 months.

Results: Most rabbits had formed a fusion mass, which was only fibrous at first, then osteofibrous and finally, in the older subjects, structured in lamellar-osteon tissue. Intervertebral foramens were negatively involved in vertebral arthrodesis, as shown by CT scans. Intervertebral discs showed irregular aspects. The increase of atresic follicles and the reduction of primordial follicles in operated rabbits led to the hypothesis of a cause-effect relationship between arthrodesis and modified hormonal status. Dorsal root ganglia showed microscopic alterations in operated rabbits especially.

Conclusions: The process of fusion mass and bone formation, associated with the arthrodesis, involves at different degrees of the vertebral bodies, discs and intervertebral foramens, ganglia and spinal nerve roots.

Key words: Computed tomography scan images, dorsal arthrodesis, histology, prepubertal rabbits, qualitative study

MeSH terms: Spinal column, arthrodesis, rabbits, computed tomography scanners, histopathology

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INTRODUCTION

Since the 1900s, the surgical approach to scoliosis has changed as thoughts and possibilities have evolved.¹⁻⁸ Nowadays, progressive spinal deformities can be

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managed with specific orthopedic devices, or vertebral arthrodesis surgery. As known, arthrodesis is not considered the best treatment for younger patients; however, it becomes almost inevitable to cure important deformities of the spine.⁹ When subjected to arthrodesis, the spine is stimulated and its response often depends on the type and extent of arthrodesis as well as on the status of the operated patient.¹⁰

In the past, experimental studies in quadrupedal mammals showed that, when subjected to dorsal vertebral arthrodesis, such animals rarely develop scoliosis, while possible natural kyphosis is reduced.^{11,12} It has then been shown experimentally in New Zealand white (NZW) rabbits that early partial or total dorso-thoracic vertebral arthrodesis affects the development of the rib cage and thoracic spine, it involves and alters vertebral values and ratios between thoracic diameters,^{13,14} while it leaves the echocardiographic values unaltered and does not reveal significant disparity in the arterial blood gases of rabbits submitted to arthrodesis and sham operated rabbits;¹⁵ other observations in dogs have reported thinning and disorganization of the growth plate.^{16,17}

This qualitative study intends to describe, with the support of radiologic imaging and light microscopy histological pictures, the extension and the morpho-structural features of the fusions taking place in the T1–T12 segment of female NZW rabbits who underwent arthrodesis, in a time period between the prepubertal age of 5–6 weeks and 17–18 months, when the experiment ended. In addition, this study admits the hypothesis that vertebral arthrodesis may have influenced on other body areas and so, it intends to verify the possible secondary involvement of other body parts, such as intervertebral discs, cervical and thoracic spinal ganglia, sternocostal cartilage, ovaries and lungs.

MATERIALS AND METHODS

Operative procedures and animal care complied with national and international regulations (Italian regulation D.L.vo 116/1992 and European Union Regulation 86/609/EC). Before proceeding with this study, the protocol was examined and approved by the Board of Directors of the Animal Facility at the Department of Life Sciences, University of Trieste, Italy. The recommendations of the ARRIVE guidelines in animals research were also referred to and taken into account.¹⁸

Animals

This study was conducted in 54 NZW prepubertal female rabbits. Thirty two rabbits underwent T1–T12 dorsal arthrodesis, while 22 were sham operated. Subjects were housed in stainless steel cages in a monitored

environment (room temperature was at 21°C with relative humidity of 40–50%, 10–15 air changes/h with a 12 h light cycle). Cages measured 0.7 m in length, 0.43 m in height and 0.53 m in depth and the cage volume was 0.17 m³. Animals were fed with a standard pellet diet (2030 Global Rabbit Diet 2030, Harlan Laboratories, Indianapolis, IN, USA) and water *ad libitum*.

Rabbits were 4–5 weeks old (range 1200–1350 g) when delivered and allowed in the Animal Facility sector mentioned above. They were given 7–9 days for adaptation, before undergoing surgery. The starting number of the 54 NZW rabbits involved in the research decreased progressively according to a schedule of planned euthanasia and such providing at different times the subject for histological study.

In accordance with this scheme, after deduction of 8 subjects (7 operated, 1 sham operated) dead during surgical procedure or during the first 3 postoperative months, 11 subjects were suppressed 2–3 months after index surgery (6 operated, 5 sham operated); 10 subjects were suppressed 4–6 months after surgery (5 operated, 5 sham operated); 9 subjects were suppressed 8–12 months after surgery (5 operated, 4 sham operated) and 16 subjects were suppressed 16–17 months after surgery (9 operated, 7 sham operated). The experiment lasted 16–17 months from the day surgery was performed. This time frame also coincides with the end of the somatic growing phase in the *Oryctolagus cuniculus*, occurring at about the age of 8–12 months, when the growth plate in long bones disappears.

Throughout the experiment, subjects were regularly weighed every 30–45 days. Identification occurred via an underskin microchip in the left leg.

Operative procedure

Surgery was performed in 32 rabbits at the age of 5–6 weeks under general anesthesia (GA) and anatomy of *O. cuniculus* was consulted in advance.¹⁹ GA was administered by an intramuscular injection of xylazine 5 mg/kg (Virbaxil® 2%, Virbac Laboratories, Carros, France) and tiletamine-zolazepam 15 mg/kg (Zoletil® 100, Virbac Laboratories, Carros, France). Subsequent skin anesthesia was obtained with a subcutaneous injection of 2% lidocaine hydrochloride (1 ml/animal).

Rabbits were operated according to a modified “Wisconsin” technique or extra-canal dorsal T1–T12 vertebral arthrodesis, corresponding to posterior vertebral arthrodesis in bipeds, as punctually indicated in previous our works.^{13–15} Multiple fragments of demineralized bone matrix (Grafton

DBM, Osteotech Inc., Eatontown, NJ, USA) were applied, during the surgery, on each side of the spinous processes of the thoracic spine to favor fusion.

The operation lasted approximately 50 min on average for each rabbit. Surgery was considered successful and at recovery from GA, the operated rabbits did not show any motor disorder.

Sham operation

Twenty two rabbits were sham operated. Access to the operating area was achieved exactly in the same manner as in those undergoing arthrodesis.

In both operated and sham operated rabbits, after lavage with saline solution, the muscular plane and the subcutaneous plane were stitched with 2/0 suture and the cutaneous plane with 3/0 suture, both absorbable (Vicryl, Ethicon Inc., USA). A sterile dressing was positioned on the surgical wound.

Postoperative care

During the postoperative period, the pain was relieved by a subcutaneous administration of carprofen (Rimadyl®, Pfizer Animal Health, West Dundee, Great Britain; 5 mg/kg twice daily for 5 days). An intramuscular injection of enrofloxacin (Baytril® 5%, Bayer Animal Health, Kiel, Germany; 5 mg/kg twice daily) was administered to prevent infection during the 1st week postsurgery.

Computed tomography scans images

Computed tomography (CT) scans were performed in 40 randomly selected animals. CT scans were obtained in anesthetized animals in supine position and were performed 7 days before surgery (t1) on 8 rabbits, 2 months after surgery (t2) on 10 (8 operated, 2 sham operated), 6 months after surgery (t3) on 11 (7 operated, 4 sham operated) and at 12 (t4) months after surgery on 11 rabbits (8 operated, 3 sham operated) to obtain objective images concerning the differences between the two groups of animals. CT scan examinations were performed with 16-slice CT scanner (Aquilion 16®, Toshiba Medical System Corporation, Tochigi, Japan) and elaborated with a postprocessing workstation (Vitrea®, Vital Images Corp., Minnetonka, Minnesota, USA). CT scan images were examined and interpreted by the specialist to assess positioning of the rods, to ascertain whether or not bone fusion and the formation of osteofibrous dorsomedian layer had occurred [Figure 1a-d].

Assessment of intervertebral fusion

CT scan images have shown the presence, or lack thereof, of thoracic intervertebral fusion, which has been assessed by semi-quantitative method, according to the following

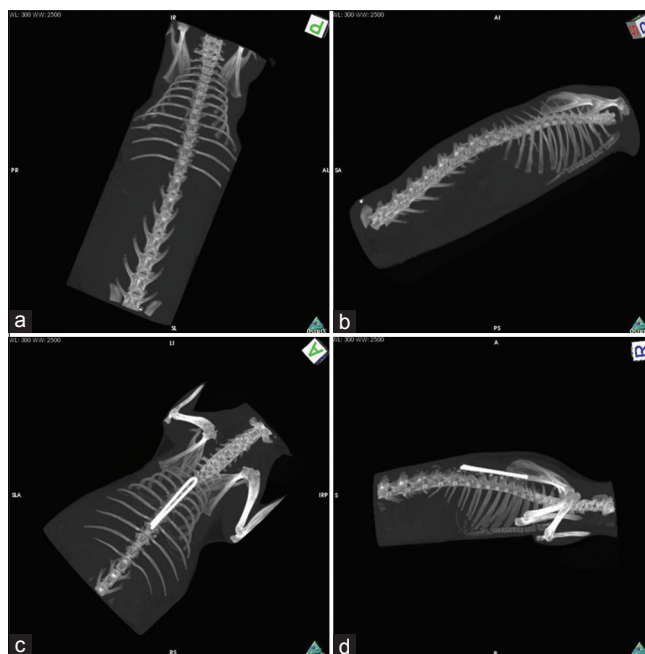


Figure 1: Computed tomography scan three-dimensional maximum intensity projection images of the thoracic area of the spine of a control rabbit; dorsal view on the left (a) and lateral view on the right (b). Rabbit submitted to dorsal vertebral arthrodesis with view of the metal rods implanted; computed tomography scan images (c and d)

arbitrary scale: No fusion (f0) when there is no evidence of osteofibrous tissue on radiographic imaging; Partial fusion (f1), when osteofibrous tissue involves a number of 5 or less thoracic vertebrae; Satisfactory fusion (f2) when scans show the involvement of the vertebral lamina and the spinal processes of 6 or more thoracic vertebrae.

Particular attention has also been made to the area taken by the intervertebral discs and to the degree of patency of intervertebral foramen.

Euthanasia at intermediate and final stages

The study required the subjects to be euthanized at different stages and submitted to postmortem examination and organic-tissue sample collection. The rabbits were first anesthetized with an intramuscular injection of xylazine 5 mg/kg (Virbaxil® 2%; Virbac Laboratories, Carros, France) and tiletamine-zolazepam 15 mg/kg (Zoletil® 100, Virbac Laboratories, Carros, France) and euthanized with an intravenous injection of embutramide-mebenzonio-tetracaine 26 mg/kg (Tanax®, Intervet Italia Srl, Peschiera Borromeo, Italy) followed by exsanguination.

Organ samples for histological preparations

Autopsy was performed to obtain samples of the ovaries, heart and lungs, the costal and intercostal muscles, the thoracic spine and related intervertebral discs, the cervicothoracic spinal cord and related ganglia. The specimens obtained

were fixed in 10% buffered formalin, embedded in paraffin and sectioned at microtome. The 6–8 μm -thick sections were stained for routine histological analysis.

In particular, the thoracic spine of both operated and sham operated rabbits were manipulated to allow the opening of the vertebral canal and extract the spinal cord and its related ganglia. The spinal cord thus obtained, which included spinal ganglia and nerve roots, was sectioned longitudinally and transversally; moreover, after removing the metal rods inserted, some of the thoracic spine of operated rabbits, previously fixed in 10% buffered formalin, was immersed in a decalcifying solution (05-03004Q, Bio Optica, Milan, Italy) for 6–8 days, postfixed in 10% buffered formalin and finally utilized to obtain specific samples regarding osteofibrous fusion mass, its two contiguous thoracic vertebrae and the related intervertebral disc.

RESULTS

Body weight

During the experiment, rabbits were weighted 13 times. Mean body weight at the time of surgery was 1612 g (range 1412–1965 g) in operated and 1654 g (range 1342–1900) in sham operated rabbits; mean body weight at the end of the experiment was 5506 g (range 4670–6150 g) in operated and 5304 g (range 4440–6100 g) in sham operated rabbits.

Computed tomography scan images

CT scan images indicate: The lack of intervertebral osteofibrous fusion mass (f0) at t1 in 8 nonoperated control rabbits and at t2, t3 and t4 in 9 sham operated rabbits [Figures 1a, b and 2a]; The presence of fusion at t2 was considered only partial in six cases (f1) and satisfactory in two cases (f2) of operated rabbits [Figure 3a]; The presence of fusion at t3 was considered only partial in two cases (f1) and satisfactory in other five cases (f2) of operated rabbits [Figures 2b and 3b]; The presence of fusion at t4 was considered absent in two cases (f0), partial in one case (f1) and satisfactory in other five cases (f2) of operated rabbits [Figure 3c].

Three-dimensional (3D) volume rendering of CT scans allowed to observe the osteofibrous layer forming simultaneously with the osteofibrous intervertebral dorsal fusion around implanted metal rods [Figure 2a and b].

The reconstruction with 3D-maximum intensity projection allowed also to assess the intersomatic spaces as well as the morphology and patency of intervertebral foramen, in order to investigate their possible involvement [Figure 3d and e].

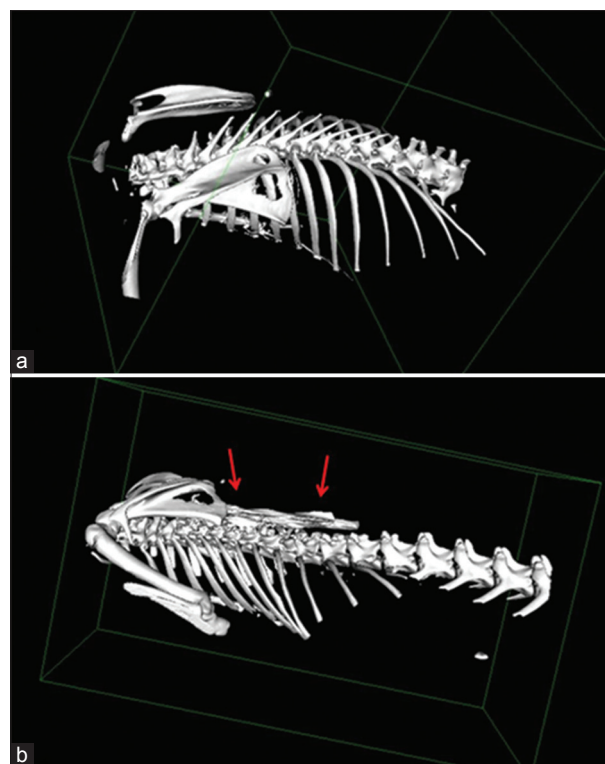


Figure 2: Three-dimensional computed tomography volume rendering reconstruction of sham operated rabbit (a) and operated rabbit (b) More clearly showing the presence of a reactive osteofibrous layer, covering the metal rods (arrows)

Histology of the arthrodesed spine, intervertebral discs and costal cartilage

The formation of an osteofibrous layer, around the metal rods implanted during surgery on the side of the spinous processes, accompanies dorsal bone fusion along more or less extended segments of the spine. Throughout this process, we have progressively documented the ossification phases and bone remodeling, together with the scan images obtained at t1–t4. In particular, the structural examination indicates: osteoblastic activity, aspects of bone deposition and osteon organization [Figure 4a–c]; increased thickness of the layer around the metal rods [Figure 4d–f]; its longitudinal extension and bone continuity between the lower plane of the layer and the dome of the vertebral canal [Figures 2b and 4f].

Areas of bone fusion between contiguous vertebral bodies were not identified. In fact, within the interspaces found between the above-mentioned areas, both the intervertebral disc and the intervertebral dense-fibrous ligaments are preserved, albeit being occasionally involved due to the arthrodesis.

Longitudinal sections of the vertebral bodies of operated and sham operated subjects allowed the examination of the cartilage located at the head or at the glenoid cavity.

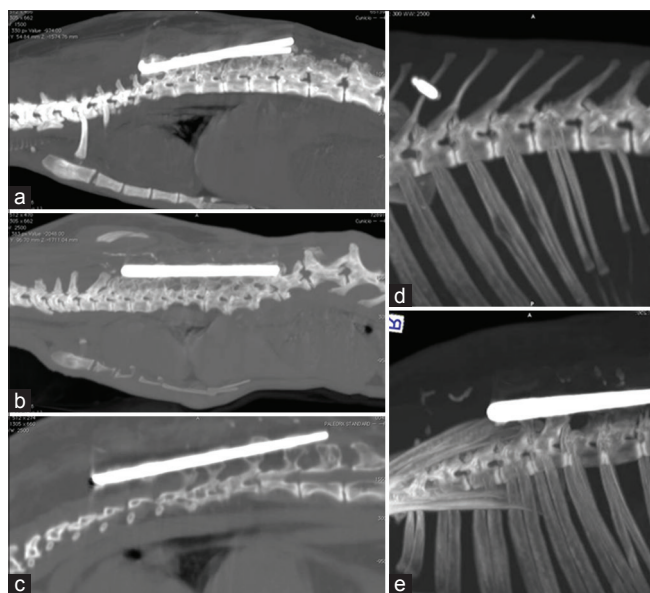


Figure 3: T1–T12 sagittal computed tomography scan reconstructions at t1–t4 showing intervertebral bone fusion. Sagittal computed tomography scan reconstruction on the left (a-c) and three-dimensional-maximum intensity projection on the right (d and e): Spaces occupied by intervertebral discs are clearly visible (d); Different view of the intervertebral foramen profile in sham operated rabbits (d) and rabbits submitted to arthrodesis (e)

In the long run, such cartilage behaves like the growth plate of the long bones, allowing the processes and the vertebral bodies to grow in length: The innermost part of its diaphyseal side undergoes an ossification process, whereas the superficial part continues to proliferate, thus determining the lengthening of the body at the end of the epiphysis [Figure 5a].²⁰ The linear aspect of this cartilaginous layer, just underneath the articular surface of the vertebra, appears altered as a consequence of arthrodesis [Figure 5b and c]. Also, the nucleus pulposus, at the center of the intervertebral disc structure, may suffer from changes in form and position due to the arthrodesis [Figure 5d and e]. Additionally, histology of the costal cartilage has revealed the presence of some natural regressive phenomena, such as asbest-like degeneration and calcification, more evident in rabbits submitted to arthrodesis [Figure 6a and b].

Histopathology of the ovaries

The prevalence of primordial ovarian follicles and the absence of cavitory or antral ones indicate that all female rabbits underwent surgery at prepupal age, before ovulation [Figure 7a and b]. Atresic follicles and residual corpus albicans can sometimes be an accentuated phenomenon, which varies depending on the ovaries and age of rabbits. The extensive analysis of ovarian follicles at different stages of folliculogenesis^{21,22} indicate a decreasing rate in the reserve of primordial and primary ovarian follicles, which seems to be more evident in operated rabbits [Figure 7c-f].

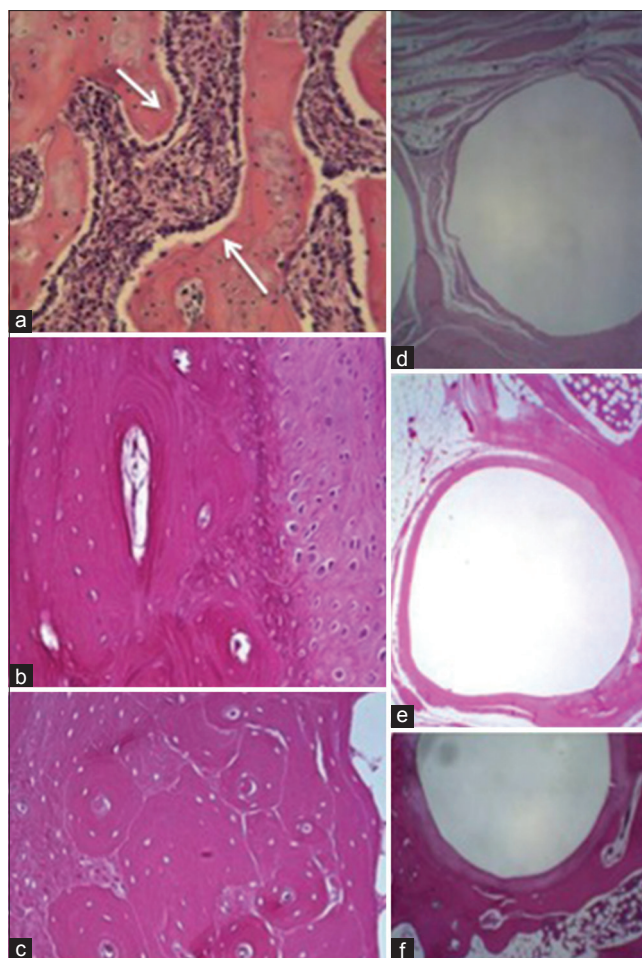


Figure 4: Morpho-structural details of the osteofibrous layer and the vertebral body (a-c), Displaying osteocartilaginous trabeculae and osteoblastic activity (c, arrows). Development of osteofibrous layer: From fibrous and bone-fibrous structure (d and e) to bone structure (f); Connection between the lower part of the bone layer and the underlying vertebral bone trabeculae (f, arrows). H and E, $\times 10$, $\times 20$ and $\times 40$ light microscopy magnification

Histopathology of the lung

The lungs of both operated and sham operated rabbits are often pathologically affected. Our observations concern rabbits from both groups who lived throughout the experiment and show in particular different degrees of congested interstice and alveolar lumina, hotspots with infiltration of parenchyma by granulocytes and lymphocytes, specific “balt” and atelectasis pictures.²¹

Spinal cord and related ganglia

Forty-one segments of cervical spinal cord, 43 of thoracic spinal cord and 543 spinal ganglia were extracted from the vertebral canal of operated and sham operated rabbits. Histological observation focused on pseudounipolar dorsal root ganglion neurons (DRGNs) of the spinal nerves and subsequently, perineuronal satellite glial cells (SGCs) and nerve fibers (NFs) of some segments of thoracic-spinal roots and nerves.

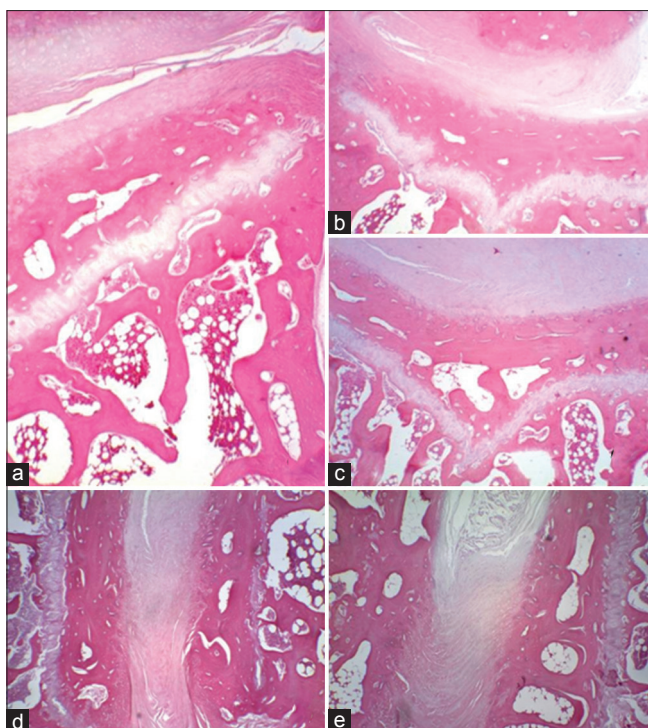


Figure 5: Linear or irregular shape of vertebral cartilage in sham rabbits (a) and rabbits submitted to arthrodesis (b and c). Morpho-structural details of the intervertebral disc: Fibrous part (d) and nucleus pulposus, partially misshaped as a consequence of arthrodesis surgery (e). H and E, $\times 10$ and $\times 20$ light microscopy magnification

The two neuronal aspects can be summarized as follows: Large neuronal bodies of rounded or at times oval shape, marked by a regular perikarion line, slightly clear cytoplasm with Nissl basophilic substance, normal aspect and distribution, round and clear nucleus and when present in the section, round and hyperchromophilic nucleolus [Figure 8b]; Smaller neuronal bodies, with irregular round or oval shape characterized by a clear perikarion line, mostly acidophilic and hyperchromophilic cytoplasm with Nissl substance poorly identifiable, oval-shaped nucleus, reduced in size, hyperchromophilic and occasionally pycnotic, an often masked and therefore hardly visible nucleolus, when present in the section [Figure 8e]. The observation suggests a state of normality for neurons in 1 and of abnormality for neurons in 2 [Figure 8b-e]. The examination of radicular motor neurons of the spinal cord does not present analogous differences [Figure 8a].

In nerves and in smaller NF bundles, the regular myelin sheath of Schwann cells and the NFs integrity in internodal zones are sometimes replaced by a swelling of the myelin sheath and by the NFs discontinuity.^{21,22} Altered expressions of DRGNs, SGCs and NFs, jointly forming the ganglion, may be signs of back pain condition.²³

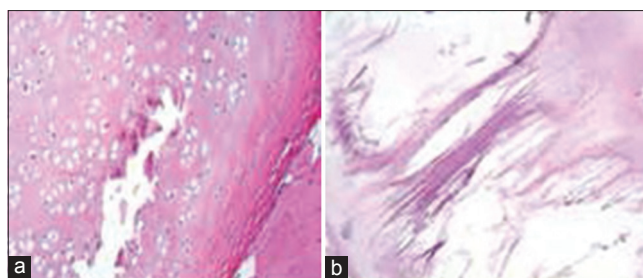


Figure 6: Areas of calcification (a) and asbest-like degeneration (b) of costal cartilage in rabbits submitted to arthrodesis. H and E, $\times 20$ light microscopy magnification

DISCUSSION

This experimental study evaluated the extension and the morpho-structural features of the fusion process in NZW prepubertal rabbits submitted to T1–T12 dorsal arthrodesis. Animals were euthanized at different times in order to verify possible secondary involvement of intervertebral discs, cervical and thoracic spinal ganglia, sternocostal cartilages, ovaries and lungs.

Compared data of the human thorax and the experimental rabbit model have clear limits determined by the model itself. However, it should not be excluded that CT scan general data and histological descriptions of the thoracic cage and spine can suggest some questions and ideas with reasonable approximation to human reality.^{11,12,21-24}

Having established and confirmed the complex implications and interactions involved in the growth of the thorax and its basic components, connected to a certain extent with arthrodesis, other observations regarding the possible involvement of other body parts, have been detailed in pathologic anatomy and so, these pose the problem of possible abnormal situations, at least, in single situations.

Given the size of the subjects, our simple arthrodesis had to be performed without including some routine operations, such as and not limited to, the removal of the superior and inferior articular facets and the derotation of the spine. Hence, response of bone tissue to attain fusion was less marked. However, despite some difficulty in some cases, most rabbits had formed a fusion mass, which was only fibrous at first, then osteofibrous and finally, in the older subjects, structured in lamellar-osteon tissue.

Despite some considerable alterations occasionally affecting the growth plate of the vertebral bodies due to the arthrodesis performed, there is no sign of fusion points between contiguous vertebral bodies with intervertebral discs interlined as barrier diaphragms. Moreover, it appears that the growth plate of the vertebral bodies,

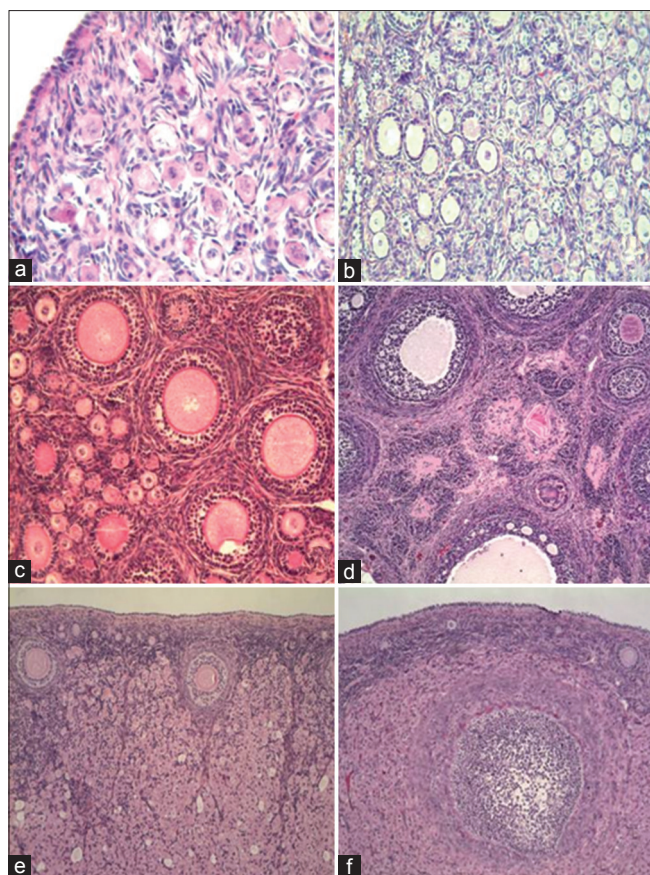


Figure 7: Noncavitary ovarian follicles in 6–8-week-old prepubertal female rabbits (a and b). Normal ovarian follicles at various stages of development (c), Atretic follicles and corpus albicans (d). Reserves of ovarian follicles in sham rabbits (e) and rabbits submitted to arthrodesis (f). H and E, $\times 10$ and $\times 20$ light microscopy magnification

with its species-related differences, ceases its function long after it disappears from the long bones, at about 8–12 months of age in the *O. cuniculus*. It is thus apparent that in humans, considering the upright posture, the trunk keeps growing even when the limbs cease to grow, with a consequent increase of height. This does not happen in quadrupedal animals as they stop growing in height, which is measured at the withers while the trunk continues to grow in length for some time.^{20,22} Well, also if it's obvious, this description points out the different prevalence of the arthrodesic strengths and gives to understand because this in quadrupedal mammals rarely develops scoliosis - while possible natural kyphosis is reduced^{11,12} - contrary to what occur in humans.

Status and physiological solution of ovarian follicles are similar in operated and sham operated rabbits. However, the increase of atretic follicles and the reduction of primordial follicles which appears to be more evident in operated rabbits leads to the hypothesis of a cause effect relationship between arthrodesis and modified hormonal status.²¹

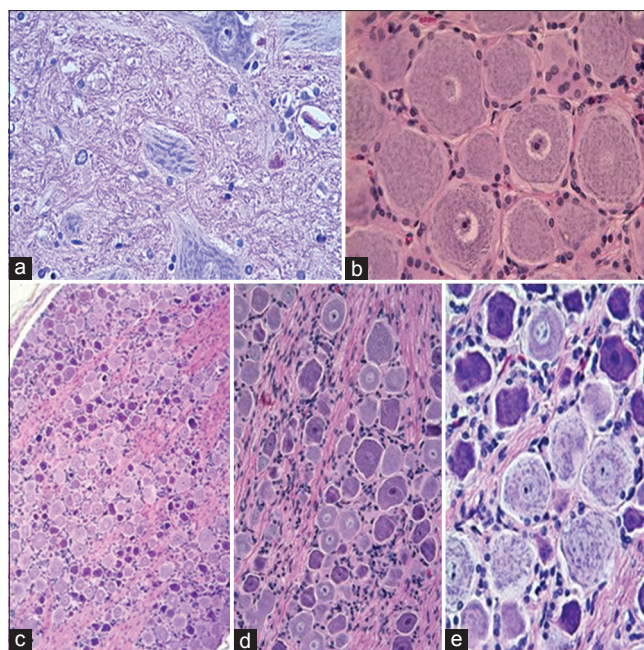


Figure 8: Morpho-structural details of central and peripheral nervous system: Motor neurons of anterior horns of the spinal cord and Nissl substance (a) dorsal root ganglion neurons of sham rabbits (b) and rabbits submitted to arthrodesis (c-e). Dorsal root ganglion neuron details (c-e) of neuronal characterization 1 and 2, as in text. H and E, $\times 10$, $\times 20$ and $\times 40$ light microscopy magnification

Given the frequent involvement of the two lungs at all ages and in both operated and sham operated rabbits and considered the multifaceted and nonspecific pathological picture, pulmonary histopathology indicates a certain tendency of the organ to develop a disease during surgery and in the immediate postoperative period, which subsequently becomes chronic.²⁵ In this regard, veterinary pathologic anatomy underlines how, in rabbits, spontaneous respiratory pathologies are quite frequent, often critical and difficult to solve.^{21,25} It is necessary to specify that the subjects examined are the ones who were euthanized last and had survived with a lung affection for 16–17 months, which can be considered quite a long time when compared to the medium life span of the species, without effects on the completion of the experiment. Lung involvement might be affected by the *O. cuniculus* species factor and secondly, by the endemic factor and presumably it did not interfere with this experimental study.

The histopathology of the nervous system recommends precision and caution in the choice and use of methods and materials, as well as in the interpretation and evaluation of the results.^{21,26} In any case, we believe this research can be continued and the contextual observations, obtained by classic procedures and regarding two structural macro-aspects of DRGNs, are acceptable.^{27,28} The structure of the DRGNs, indicated as 2, can be interpreted as a response to both the arthrodesic implant

and surgery of operated and sham operated rabbits. Some authors suppose that, after receiving nociceptive stimuli, an organism as a whole is capable of inducing subtle morpho-structural changes in the DRGNs, although they do not hint to the existence of multiple neuronal populations. It has been reported that axotomy and target deprivation frequently induce standard apoptosis, or in some cases autophagic neuronal death involving strong endocytosis and cytoplasmic cell death. Moreover, light microscopy observations in rats show that, at 12 weeks after axotomy and surgical repair, some of the neurons in the DRGNs displayed dramatic morphological changes.^{29,30} There are studies supporting the existence of a second, albeit modest, population of atypical neurons, morphologically recognizable applying histological routine, of dorsal root ganglia.³¹ Finally, other authors have related lumbar herniated disc to age, presenting a possible and plausible interpretation of the consequent inflammatory response and neuronal ganglionic damage of the dorsal root.³² Moreover, pathological anatomy devotes a considerable number of chapters to regressive and inflammatory alterations of the peripheral somatic and visceral nervous system. There is a consistent number of studies by several authors that have consolidated with time and that can support more recent data.²⁸ We believe that one of the two morpho-structural characterizations of “T-shaped” neurons, presented in point 2 could express, as from our considerations, the response of certain DRGNs after receiving peripheral stimuli, initiated by surgery and arthrodesis. Neurons with morpho-structure 2 are present at different percentages or can be almost completely absent in the ganglia of rabbits submitted to arthrodesis and sham rabbits, suggesting that, in any case, surgery would not be inoffensive for both groups and that in the long term their number may vary and decrease, recovery may not be complete and the peripheral afferent stimuli may have different intensity.

The SGCs are normally disposed in monolayer at the peripheral surface of the pseudounipolar body neurons [Figure 8b].^{33,34} The increase in number of SGCs and their irregular distribution in “onion bulbs,” can be interpreted as a response to back pain and lower back pain.^{23,24}

Intervertebral foramen, although in an extremely variable way, can be negatively involved in vertebral arthrodesis, as shown by CT scans: Such data are useful to explain how impairment and traumatic-compressive damage may occur on the spinal nerve fascicles exiting the intervertebral foramen.

Our partly inevitable conclusion brings us to positively evaluate the observations and suggestions provided by the

experimental model *O. cuniculus* as they underline some yet unresolved issues, regarding:

(a) The growth plate of the vertebral body, which stands as a critical aspect in the development of the vertebrae in arthrodesis situations (b) Regressive phenomena of costal cartilage, which represent possible limiting factors for the plasticity and flexibility of the entire thorax;¹⁴ (c) Histopathological alterations of the ovaries following arthrodesis are possible (d) Spinal ganglia with pseudounipolar neurons and their SGCs, can be potential reactive centers related to back pain as they collect multiple, different peripheral afferent pathways.³⁵⁻³⁷

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Nil.

Conflicts of interest

There are no conflicts of interest.

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