ESOPHAGUS STRICTURES: LATEX-DERIVED FLOW MECHANICAL CONTROLLER

Suélia de S. Rodrigues Fleury Rosa, suelia@unb.br
Universidade de Brasília (UnB), Faculdade UnB Gama (FGA) – Área Especial 2 Lote 14 Setor Central, Caixa postal: 8114, CEP 72405-610 – Gama – DF

Adson Ferreira da Rocha, adson@unb.br
Universidade de Brasília (UnB), Faculdade UnB Gama (FGA) – Área Especial 2 Lote 14 Setor Central, Caixa postal: 8114, CEP 72405-610 – Gama – DF

José da Conceição Carvalho, carvalhorh@gmail.com
Faculdade de Medicina, Departamento de Ortopedia e Cirurgia Plástica – Universidade Federal de Goiás – Hospital das Clinicas (HC-UFG). 1ª Avenida, s/n – Setor Leste Universitário – 74605-020 – Goiânia – GO

Alberto Lopez Delis, lopez_delis@yahoo.com
Medical Biophysics Center, University of Oriente, Santiago de Cuba, Cuba

Rafael Moreira Messias, messiasunb@gmail.com
Universidade de Brasília (UnB), Faculdade Tecnologia, Campus Darcy Ribeiro, CEP 72900-910 – Brasília – DF

Abstract. *This paper reports on the development of a new mechanical device: the latex-derived esophagus flow controller. The device is based on a pre-existing concept which is applied in all currently used obesity treatment techniques and in devices used routinely in hospitals. The esophagus is an organ whose function is to allow the passage of food. The purpose of the latex flow controller is to reduce the lumen of the esophagus mechanically. The raw material for this device is natural latex, extracted from the Hevea brasiliensis tree. This natural latex flow controller presents ideal characteristics for future application in the control and treatment of obesity.*

Keywords: *esophagus, latex, obesity.*

1. INTRODUCTION

The reactions of the body from the beginning to the end of the feeding process are divided into three stages: the cephalic phase, prior to the intake process, in which visual and aromatic stimuli influence the nervous system, causing an increase in saliva secretion and gastric juice; the gastric phase, which includes the mastication and swallowing process; and the substratum phase, in which the food undergoes partial digestion in the stomach and goes down to the intestines (Guyton and Hall, 2002).

The hormones that are delivered when the food enters into contact with the stomach and the intestine are also part of this process. They enter the bloodstream where they perform different functions and affect the digestion of nutrients through mobility, secretion and absorption (Demaria, 2005). These hormones, produced by the digestive system, act on the cerebral centers that balance appetite and satiety and determine our daily calorie intake, Smell and taste stimuli from food also help regulate ingestion. All these peripheral signs are integrated in the nervous system with the consequent delivery of neurotransmitters (Fobi and Fleming, 1989).

Studies have shown that due to integration and correlation in the digestion process, obesity treatments, both non-surgical, involving the use of intra-gastric devices or reducers, and surgical, with changes in digestive treatment, have caused functional sequels (Hojo and Nobre, 2007). Food intolerance is observed, with associated regurgitation, infections, dehiscence, and stenosis of the stomach. In the long run, nutrient deficiencies, particularly of vitamin B12, folic acid and iron, may affect ingestion and satiety hormones such as ghrelin and leptin (Capella and Capella, 2003). Changes anywhere in the digestive tract will cause some dysfunction, and this is the main drawback to current obesity treatments.

In the digestive system, the esophagus allows for the passage of food and does, not participate in any absorption process. Interestingly, there are clinical reports of esophageal diseases that indirectly cause weight loss. The objective of this article is to present a preliminary proposal for a *Hevea brasiliensis*-derived latex flow controller applied in the esophagus.

2. METHOD CONCEPT

2.1. Esophagus Structure

The esophagus is a muscular tube that is continuous with the laryngeal portion of the pharynx and covered by a paving stratified non-keratinized epithelium. The esophagus consists of striated muscle (voluntary control) in its upper third, smooth muscle (involuntary control/ peristaltic movements) in its lower third and a mixture of striated and smooth muscle in the middle third. In the esophagus the presence of the upper esophageal sphincter (UES) and the lower esophageal sphincter (LES) prevents the entrance of air and gastric contents, respectively. The esophagus is approximately 25 cm long from its origin, at the level of the sixth cervical vertebra, to the esophageal-gastric junction located at the level of the eleventh thoracic vertebra. The esophagus begins about 15 cm from the incisors and ends about 38 cm away from them. It has a 3 to 4 cm diameter in an adult, depending on the individual's build.

The esophagus can be classified as cervical, thoracic or abdominal depending on location. Along its pathway, it is linked to certain structures that can compress it and reduce its lumen. These structures are, from top to bottom, the cricoid cartilage (at the level of the sixth cervical vertebra), the aortic arch (in the upper mediastinum), the main left bronchus (right below the aortic constriction) and, finally, the diaphragm, which allows the passage of the esophagus through the esophageal hiatus.

2.2. Digestion

When leaving the mouth, food enters the pharynx, whose main function is to conduct air to the larynx, windpipe and lungs. However, its directional constrictor muscles along with the epiglottis also accomplish the deviation of food into the esophagus. The food arrives at the esophagus, which acts only as a conductive tube, leading the food from the mouth into the stomach. When food arrives, the upper esophageal sphincter (UES) relaxes and allows the passage of the food into the esophagus. A peristaltic wave initiated in the pharynx travels the length of the esophagus. The lower esophageal sphincter (LES) relaxes to transmit the food into the stomach. Through peristaltic movements in the esophagus, food arrives at the stomach. Besides linking the oral cavity with the stomach, the esophagus, is responsible for the continuation of the deglutition initiated in the mouth, in other words, for food transmission. Deglutition may start voluntarily, but, soon after, it is almost completely under a controlled reflex. The deglutition reflex is an orderly sequence of events that impel the food from the mouth to the stomach. It also inhibits breathing and prevents transmission of the food into the windpipe during deglutition.

2.3. Conditions

Esophagus conditions in the literature that interest us relate to the pharynx, lower esophagus ring, and esophageal membranes, and include lusory dysphagia, stenosis, esophageal cancer, and achalasia (cardio spasm, esophageal aperistaltism, and mega esophagus). The most common symptom of esophageal conditions is dysphagia. This is, a sensation of difficulty in swallowing a sensation that food is not progressing normally from the pharynx into the stomach or that it is retained somewhere along the way. Odinophagia is the painful sensation that occurs when the movement of liquids and solids is impeded by physical abnormalities of the pharynx, of the esophagus and of the neighboring organs or by problems of the nervous system or muscular problems caused by such conditions. The difficulty in swallowing leads to weight loss, a condition common to sufferers of all of the above mentioned conditions. As important as weight loss as an indirect sign are the kinds of treatments for many of the conditions already mentioned, such as mechanical dilation through balloons inflated inside the esophagus. Often, a number of interventions are made, and, in some cases, the balloons stay inside the esophagus for up to 48 hours.

2.4. Flow Controller

To control and treat obesity one tries to limit the volume and flow of food intake. The overload of nutrients ingested by the obese individual is favored by a high esophageal flow which allows the passage of food at low resistance. The common aspects observed in diseases of the esophagus lead us to conclude that high resistance (smaller esophagus diameter) causes weight loss. By reducing the diameter of the esophagus, esophageal flow can be reduced, limiting the type and amount of food that can be ingested.

A mechanical system placed in the esophagus reduces its effective radius, slowing the flow of food being consumed. With a nearly cylindrical format, the latex flow controller contains a central lumen, with a diameter considerably smaller than the diameter of the esophagus, which limits the rate of food passage through the organ. Made from the natural latex extracted from the *Hevea brasiliensis* rubber tree, the controller has biocompatibility characteristics when processed appropriately (MRUE 1996). On the basis of existing techniques and objects used in the medical field, an experimental model called an esophageal flow controller module (EFMC) was developed. A physical model and a new raw material for this application were proposed in order to control the flow of food in the esophagus.

Manufacturing the EFC module

The raw material that was chosen was extracted from natural rubber latex, *Hevea brasiliensis*. From the natural latex, a final compound was prepared that has given the EFC module the essential characteristics of elasticity, smoothness, as well as being waterproof and hypoallergenic. This compound was achieved by the addition of chemicals in accordance with Mrue 1995. The module was prepared by taking the following steps: filtering and further dilution of the compound in bi-distilled water at a temperature of 20 ^{O}C.

The module, shown in Figure 1A, was designed to fit the anatomy and characteristics of the wall tissue of the esophagus of a dog, especially the longitudinal grooves of the esophageal mucous membrane (Mrue 1995). It has three distinct elements: the external and internal tubes, and the valve. This shape was proposed in such a way that the module could be submitted to a suitable pressure and have a coefficient of friction sufficient to keep the module positioned against the esophagus wall, without the need of another support technique. The mould used for forming the external tube of the module was made from tubes of Tecnil (manufactured by DRACMA, São Paulo, Brazil), with dimensions of 15cm in length and 2cm in diameter, having eight external longitudinal grooves. This mould, with latex in its wall, is shown in Figure 1A. The mould used to form the internal tube was a glass tube containing boron-silicate (manufactured by NORMAX, Marinha Grande, Portugal) with a 1cm external diameter. This mould, with latex in its wall, is presented in Figure 1B. The valve was also made of latex, and was formed by a more complex process. It has a structure that is similar to the valves used in soccer balls.

The moulds were previously cleaned and sterilized in an autoclave, and then received successive, gradual and uniform baths, followed by drying periods, until a latex compound was obtained. The moulds were first immersed in latex and then subjected to a temperature of 70°C, in a thermostatic oven, for curing, in five-minute intervals. Then, the thermostatic stove was turned off for 20 minutes, and, in this period, the mould remained inside the stove. These steps of bathing and drying were repeated until a thickness of 2 mm of the external module and 1.5mm at the surface of the glass tube were reached. After the internal and external tubes were ready, these two parts were assembled one inside the other. The module remained for 24 hours at room temperature for the process to be finished. Then a 27G scalp (Embramed, Cotia, Brazil) was introduced in the valve of the EFC to be used in the filling of the module. After placing the scalp, three more latex immersion baths were performed with subsequent heating in the stove, to finally obtain the EFC module for final implementation. An electronic system, with a man-machine interface, was especially projected to inflate the EFC. This machine contains a pressure sensor with a precision of 1mm Hg, and it allows the automatic inflation of the module using carbon dioxide (CO_2). The doctor chooses the desired pressure value through commands on the screen. When the module was finished, it was submitted to visual inspection for detection of defects. As such, tests were done for assessing wall resistance and deformation in the walls after inflation under pressures of 80mm Hg and 100mm Hg. A subsequent immersion in water allowed the search for leaks.

Test of the EFC in a dog

The testing procedure was approved by the committee of ethics in research of the Federal University of Goiás. The animal was previously subjected to the procedures for vaccination, control of ecto and endoparasites, in addition to laboratory tests, hematology and clinical chemistry, for verification of its health. The module was inserted, by endoscopy, in a male adult mixed race dog, with a body weight of 12.7 kg. The application of the module was preceded by food restriction of 12 hours. Diazepam was used in pre-anesthesia in the proportion of 0.5mg/kg and the anesthesic propofol, in the proportion of 6.0mg/kg, for induction, and 0.5mg/kg/min to maintain anesthesia, all done intravenously. Before the examination, under food restriction of 12 hours, the animal was anesthetized with the association of cloridrates levomepromazine, tiletamine and zolazepam at doses of 0.5, 2.5 and 2.5mg/kg per body weight, administered intramuscularly, all in the same syringe. After loss of reflexes, the animal was subjected to endoscopic examination, initially to assess the physiological macroscopic conditions and anatomy of the esophagus, then, the unfilled EFC module was placed. The module was introduced slowly and positioned between the atlas and the fourth cervical vertebrae. Once in the desired position, the module was slowly inflated until it reached the specified pressure of 60mm Hg. The scalp was carefully removed to prevent damaging the esophageal wall and pressure loss in the module.

Later, the animal received a puréed diet in liquid form prepared in a blender in the proportion of 400g solid food to 1 L of water. The amount provided was calculated according to the body weight of the animal, as instructed by the manufacturer of the dog food. During the seven days subsequent to the placement of the module, the behavior of the animal was evaluated by a veterinarian for food ingestion, vomiting, coughing and loss of body weight with observations recorded daily on the dog's chart. To confirm the continuation of the module's positioning, radiological examinations were performed on the latero-side incidence of the right cervical region immediately after the placement of the module and two days from the withdrawal of the module. The removal of the module followed a protocol that was very similar to the one used for its placement.

3. RESULTS AND DISCUSSION

The EFMC is made of natural latex with the addition of chemical substances. The objective was to give the product characteristics indispensable for flow control: elasticity, softness, resistance, impermeability and hypo-allergenicity. In the production process successive immersion baths were used. Molds were gradually and uniformly placed inside the latex perpendicular to the plane and then heated in a thermostatic stove.

The molds, which were made of *tecnil* (polyester), glass and aluminum gave better results than did glass-only molds, because little adherence with of glass. The shape of the molds was determined by the anatomy and characteristics of the esophagus tissue wall the objective was to obtain a high friction coefficient but without causing uniform pressure on the tissue wall. Two molds were the result, one a wrinkled mold with concentric circumferences and another with evenly spaced longitudinal grooves. Both molds were tested, and the one with longitudinal grooves presented better results.

In making the module, the molds had been previously washed with soap and water, hot-air dried and sterilized in an autoclave. They were heated in a thermostatic stove to 50 °C, removed, immersed in the latex through the immersion bath, and left inside the composition for 1 minute. At this point polymerization, which produced the module, began, after polymerization, the modules were removed slowly and gradually, placed inside the thermostatic stove and heated to 100 ºC at five-minute intervals for vulcanization. After that, the thermostatic stove was turned off and the molds were left inside for 20 minutes. Immersion and heating were repeated until a thickness of 2.5 mm was obtained for the external module and a thickness of 1.5 mm for the tube surface and the radiographic indicator. After this vulcanization period, the module was left for 24 hours at room temperature to complete the production process. The valve was made in the same way as the other three parts.

However, it took an, average of three days to complete, because the 0.5 mm thickness between the stems had to be very well vulcanized, demanding a more meticulous production process. Under running water, the module pieces were removed from the molds, that is, the layer of latex was slowly removed to avoid damaging it. After the separate pieces were made, the next step was to assemble the EFMC. At this stage, the valve was glued with latex to the internal tube. This was carefully done with a syringe to avoid slippage, and the piece was then placed in the thermostatic stove at 100 ºC until it had firmly adhered to the tube. After this stage, the internal tube was bathed three more times to fix the thread and placed again in the thermostatic stove. After drying, the tube with the valve and radiographic indicator were dressed by the external module, and the ends were closed with latex in a process similar to the one described previously. At this point, a 27-G scalp was placed in the EFCM valve to inflate the module. After scalp placement and three more latex immersion baths, the unit was heated in the thermostatic stove as in the previously described procedure; see Figure 1.

Figure 1: Photograph of the Esophageal Flow Controller Module - EFCM, from left to right; upper and side view.

Once the characterization process was completed, the module was sent for sterilization. The modules were packed individually, labeled with their physical dimensions and properties and then sterilized in ethylene oxide. A micro-controlled system, which is a man-machine interface, was developed to fill the EFCM with carbon dioxide gas (CO_2) automatically. Using a screen command, the doctor types in the pressure that will be used and the system does the inflating. The desired value is obtained through a pressure sensor with a 1 mmHg tolerance range. The newly developed device provides appropriate elasticity and the properties of vulcanized latex would allow it to be applied inside an organism without changes or allergic reactions. Thus, this new device can mechanically reduce the esophageal lumen and limit both the amount and kind of food ingested. To analyze the module's structural properties, tests were carried out to evaluate the performance of the module and to establish its range of use. In accordance with the established manufacturing procedures, the model presented here has the capacity to hold air without leaks or ruptures at maximum pressure. Structural uniformity is maintained at the pressure used and the valve's expected life is satisfactory for the specified application. A simple ASTM-referenced test showed that the EFCM's thermal behavior was similar to that of other latex compounds mentioned in the literature. Further research will seek to completely characterize the device and test it on animals and humans to validate this new applied restrictive device for the control and treatment of obesity.

The dog was submitted to a food restriction of 12 hours as a prophylaxis for vomiting in the trans-anesthetic, given that it could interrupt the endoscopy procedure and cause discomfort to the animal. Moreover, this procedure prevents a potential cause for the development of pneumonia caused by aspiration. The result of the application methodology through endoscopy was positive because it promoted the evaluation of the integrity of the esophagus prior to the placement of the module. Also, the use of this technique facilitated the installation of the module in a slow and monitored way that allows for accurate positioning without damaging the mucous membrane. Through video-endoscopy, the module in the esophagus was shown on the computer screen, reducing its diameter from 3cm to 1cm.

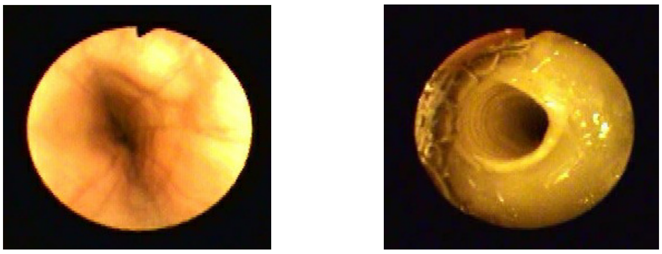

Figure 2: (**A**) Photo of the endoscopic appearance of the dog's esophagus wall. (**B**) EFC Module with 60mm Hg in the esophagus.

In the seven days following the placement of the module, its retention within the esophagus was accompanied by x-ray examinations and a perfect accommodation between the atlas and fourth cervical vertebrae was found. The radiographic visualization of the piece was possible because the esophagus was distended by the presence of the module filled with gas and can be seen in a radiolucent image in the dorsal trachea, Figure 3. After the application of the module, the dog was put in an individual cage and its recovery from the procedure was monitored. In the first 15 hours there was salivation, coughing and isolated events of moderate choking. Such occurrences were possibly related to the period of the esophagus accommodating the object inserted in lumen. After the first meal, a radiographic exam was made to check the position of the EFC module. The result of the exam confirmed positive expectations, indicating, among other things, that the consistency of the food was appropriate to pass through the inner portion of the module without sending the module to the stomach. The quality of the food could also be assured. In subsequent evaluations of the animal, excessive salivation, episodes of regurgitation or apparent discomfort in the animal were not observed. During the seven days there were no changes regarding the intake of food, vomiting and coughing. This data suggest that the size of the module, the pressure on the walls of the esophagus and the place of installation were appropriate for maintaining the device in a dog of medium size with a body weight of approximately 12 kg. After seven days, the animal was again subjected to a video-endoscopy exam for the removal of the module. During the examination it was observed that the module was properly positioned, confirming what was seen on the x-rays. Moreover, the presence of food remains wasn't observed in the cranial portion of the esophagus or around the module.

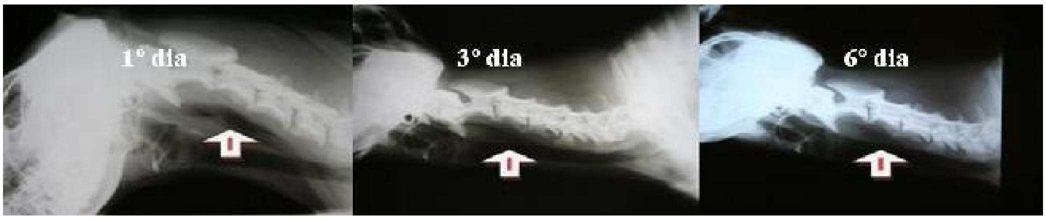

Figure 3: Lateral radiographic images of the cervical region of a dog, registered on the first, third and sixth days after the placement of the EFC. The arrow indicates the radiolucent area, interposed between the cervical vertebrae and trachea, which corresponds to the region in which the module is positioned in the esophagus.

After the removal of the module, no damage to the wall of the esophagus was found along its length. Meanwhile, during the process of removing the EFC module, which was inflated using a pressure of 60mm Hg, some difficulty was encountered because it was very slippery. In the process of introducing the endoscopic nippers to pull the module out, the module slipped and lodged itself in the stomach of the animal. Ten days after of that occurrence, the EFC was expelled orally and it was observed that its integrity was seriously compromised. It is believed that other animals that were living with the dog may have bitten and damaged it.

Analyzing the issue of the module's displacement, it can be assumed that the application of a long nylon wire introduced in the module could be used for external fixation at the same region in the side of the face or the animal's neck. This procedure could be tested in order to prevent the device moving to other regions of the esophagus or even into the stomach. Considering the variable of weight loss during the experiment which wasn't the main target as other data and conclusions were the objectives of this research, there was a weight loss of about 4% during one week of observation. However, this result should be carefully checked and validated in further studies using this approach. Nonetheless, these preliminary results are encouraging and are a good justification for the testing of this new method in a larger group of dogs in order to track various other parameters related to the module and the physiology of the animal.

4. CONCLUSIONS

The new system presented here will certainly result in a new product with applications in the treatment of obesity since it is based on treatment concepts already applied to humans; this can be a new method of treating human obesity that will control food intake through mastication reeducation.

However, as an initial point of departure for the research and the development of a new treatment technique for control of a disease, these initial studies and the presentation of the applied concept are necessary so that there can be no doubt about what this proposal entails.

5. ACKNOWLEDGEMENTS

This work was financially supported by a grant from the Brazilian Ministry of Education –MEC/CAPES, Fátima Mrué for invaluable assistance and guidance in the use of latex and Universia-Santander with Premium Biotechnology National.

6. REFERENCES

Capella J. F., Capella R. F., 2003, “Bariatric Surgery in Adolescence. Is this the Best Age to Operate?”, In Obesity Surgery, ISSN 0960-8923, 13:826-832.

Demaria E.J., 2005, “Surgical options for obesity”, In Gastroenterol Clinic North American.; Vol. 34 pp. 127-142.

Fobi, M. A. L., Lee, H., Fleming, A. W., 1989, “The surgical technique of the banded Roux-en-Y gastric bypass”, In Jounal of Obesity & Weigth Regulation, ISSN: 0731-4361 Vol. 8 pp.99-102.

Guyton A. C., Hall J. E., 2002, “Tratado de Fisiologia Médica”, Guanabara Koogan S.A . Brasil, 10nd edition, 631p.

Hojo V. E. S., Melo J. M., Nobre L. N., 2007, “Alterações hormonais após cirurgia bariátrica”. In Revista Brasileira de Nutrição Clínica; Vol.22(1) pp.77-82.

Mrué, F., 1996, “Substituição do Esôfago Cervical por Prótese Biosintética de látex: estudo experimental em cães”, Ribeirão Preto, 1996, 114p. Dissertação de Mestrado Faculdade de Medicina da Universidade de São Paulo, FMRP/USP.