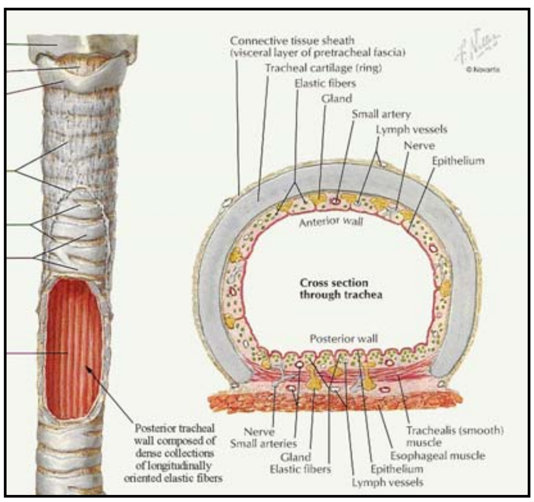
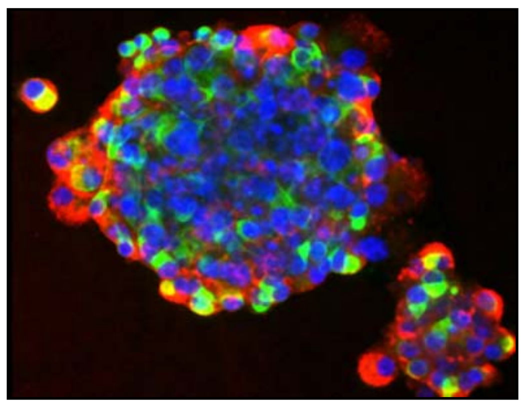
T^4

TRACHEA, 3-D, TORS, TRANSPLANT





LEGOS 4 THE CURE

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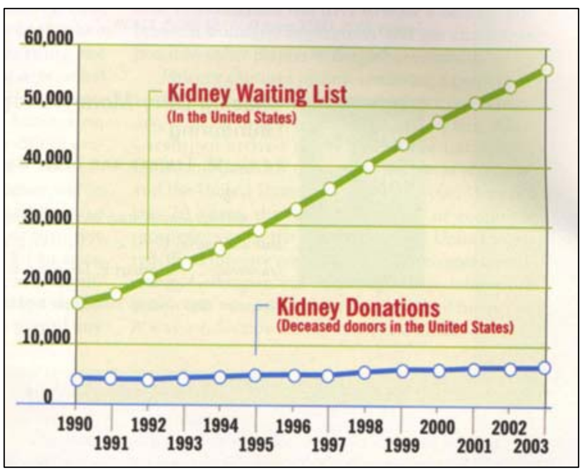
We are the FLL team LEGOs 4 the Cure. This years theme for the FLL competition, “body forward”, focuses on bioengineering. The subject we chose for our research project is applying current and future technology to help patients who require a tracheal transplant.

According to Dr. Lisa Milkowski, and John Janik, the cost of treating patients with organ or tissue failure accounts for approximately 50 percent of total annual healthcare costs in the United States. Also there are many problems with this type of surgery. One question we asked was, why can't we just use an artificial trachea? It turns out that there are several reasons. The survival rate for tracheal prosthesis transplant patients is very low as you can see from this data table and we learned that the surgery takes a long recover from and that some patients require a permanent feeding tube. Organ shortages are also a growing problem. In the last 20 years, kidney shortages have jumped up 75% according to the University of Missouri. We think that this may reflect the amount of other organ



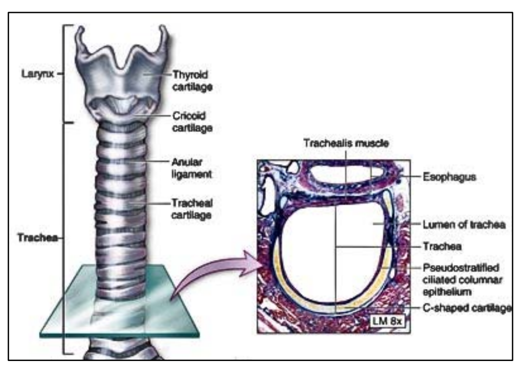
4 *Toomes, Mickisch, Vogt-Moykopf*

Table 2 *Clinical data on nine patients treated with a Neville prosthesis*

atient o	*Age*	*Sex*	*Pathology*	*Location*	*Operation*	*Survival time*	*Complications due to prosthesis*	*Cause of death*
	49	M	Squamous cell carcinoma	Middle third	Resection 7 cm, straight prosthesis	2 m		Tumour
	29	F	Malignant melanoma metastasis	Distal trachea and bifurcation	Carinal resection, bifurcated prosthesis	4 m	Sputum retention	Tumour
	55	M	C cell thyroid carcinoma	Upper and middle thirds	Resection 9 cm, caval patch, bifurcated prosthesis	10 d		Cardio-respirator insufficien
	55	F	Malacia (previous lymphosarcoma)	Middle third	Resection 6 cm straight prosthesis	15 d	Erosion haemorrhage	Erosion haemorrh
	55	M	Cylindroma	Upper and middle thirds	Resection 8 cm straight prosthesis	7 m	Loosening of prosthesis	Septicaemia
	54	M	Progressive perichondritis	Upper and middle thirds	Resection 6 cm straight prosthesis	10 m	Sputum retention, loosening of changing of prosthesis	Erosion haemorrh
	58	M	Squamous cell carcinoma	Right main bronchus and carina	Pneumonectomy, carinal resection, straight prosthesis	4 m		Tumour
	50	M	Cylindroma	Bifurcation	Carinal resection, bifurcated prosthesis	13 m (alive)	Granulation tissue, laser coagulation	
	63	M	Squamous cell carcinoma	Right upper lobe and carina	Carinal resection, bifurcated prosthesis	8 d	Sputum retention	Cardio-respirator insufficien

shortages.

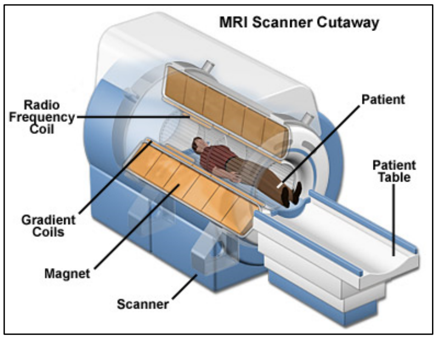
While coming up with this solution we had to learn about the anatomy of the trachea. The trachea has four layers. The innermost layer is made up of pseudo stratified cilliated columnar epithelial cells. They are covered with mucus and the cilia push the mucus upward in order to remove debris



from the trachea so you can swallow it. The next layer is the submucosa which creates mucus and stores it in goblets cells. The ridges you feel on your trachea is the cartilaginous layer which gives the trachea its form, and the outer layer connects the trachea to the esophagus and the larynx.

Our solution is to custom grow a trachea for each patient. Below we will outline our proposed procedure.

We would begin by using an MRI machine to scan the patient's trachea. The MRI machine



creates an electromagnetic field and uses it to align all the protons in the human body. It uses RF coils, or Radio Frequency coils, to send and record the reaction of the protons thus making a two dimensional cross section. According to the website 3D-Doctor, these cross sections can be combined to create a 3D computer model.

This model can then be used by a sterolithography 3D printer to create a biodegradable model that is an exact copy of the inside of the patient's trachea. The 3D printer will use the matrix created by the MRI created model to lay down very thin layers that will create this matrix.

Once we have this matrix we can use a bio-printer to print stem cells onto it. Gabor Forgacs and his team from the University of Missouri, have used the bio-printer to create blood vessels, which are layered like the trachea, so it seemed very probable that it would be possible to print a trachea. The University of Missouri separates the cross sections printed with bio-paper. Our idea was to use the model created by the MRI scan and the 3D printer to grow the matrix on.

Next we will send hydrogel through the form to allow the cells to sort themselves. The way these cells sort themselves is through the Differential Adhesion Hypothesis. This theory was developed by Malcom Steinberg. It states that similar cells prefer match up with each other. This has been tested many times, and it is a fact that cells with similar adherent properties prefer to match up with each other.

The traditional way stem cell tracheae are grown, is to implant them into the patient's abdomen or arm. This way has worked in many patients, but there are other options if the patient doesn't want to have the trachea implanted in to them. One way is the ORGANIZER^{tm} Series 100 “In breath”. This bioreactor, developed by Harvard apparatus helps grow tracheae in a more advanced way. It bathes the growing trachea in a solution that feeds oxygen to the cells at the same time it carries away the waste This takes place out of the patient, so the patient doesn't have to worry about damaging their trachea.

When the trachea is grown, it can be transplanted using the TransOral Robotic Surgery system, a robot developed originally to work on lungs, but is currently being used for removing cancerous tumors, and helping with sleep apnea. We are somewhat familiar with the TORS system and believe that if it were modified with smaller instruments on the arms, so the arms could get into the trachea, and the arms were at an angle to come in through the throat instead of the abdomen, it could used to preform our surgery. This has many advantages for both the patient and the surgeon. One of the features it has for the surgeon is a console that the robot is controlled allowing the doctor to be anywhere in the world, also the instruments are programed to be precise, and not vibrate, even if the surgeon's hands vibrate. Some of the advantages for the patient is the fact that it requires no incision, instead of breaking the patient's jaw and making an incision from the patient's ear down their neck. Also there is way less recovery time with this type of surgery, and the risk of being required to have a breathing or feeding tube is minimal.

Conclusion

We are aware that much of our proposal is based on new but existing technology. We do believe that the way we combine these technologies with our idea of building a bio-degradable custom fit matrix for each patient is new. These ideas combined with using a robotic surgical system to carry out the actual transplant, make our proposal unique.