Team 5: NanoBolt™

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Clinical Problem

- Osteoid Osteomas
    - Small benign bone tumors
    - Typically affect children and young adults
    - Account for 11% of all benign bone tumors (~450,000 cases per year)
    - Cause pain and discomfort
- Current Solutions
    - Surgical Resection
        - High risk of complications
        - Increased risk of fracture
    - Thermal Ablation
        - Microwave or radiofrequency
        - Ablation zone size of 5-7 cm
        - Average size of osteoid osteoma = 1-2 cm
        - Increased risk of damage to healthy bone

A. Julka, P. Jebson, and M. Tomaino, "Common Benign Tumors of the Hand," *AAOS,* Aug. 2015. https://www5.aaos.org/OKOJ/vol13/issue8/HAN055/?ssopc=1

https://www.youtube.com/watch?v=gGn3XhZBSQA

https://www.jnjmedicaldevices.com/en-US/product-family/neuwave-microwave-ablation-systems

Need Statement: A way to minimize the ablation zone size of a nanosecond pulse electric field (nsPEF) ablation system in order to target smaller tumors such as osteoid osteomas laparoscopically.

Market and FDA Regulation

TAM: Total US Bone Tumor Population

SAM: Benign bone tumor cases

Target: Osteoid osteoma cases

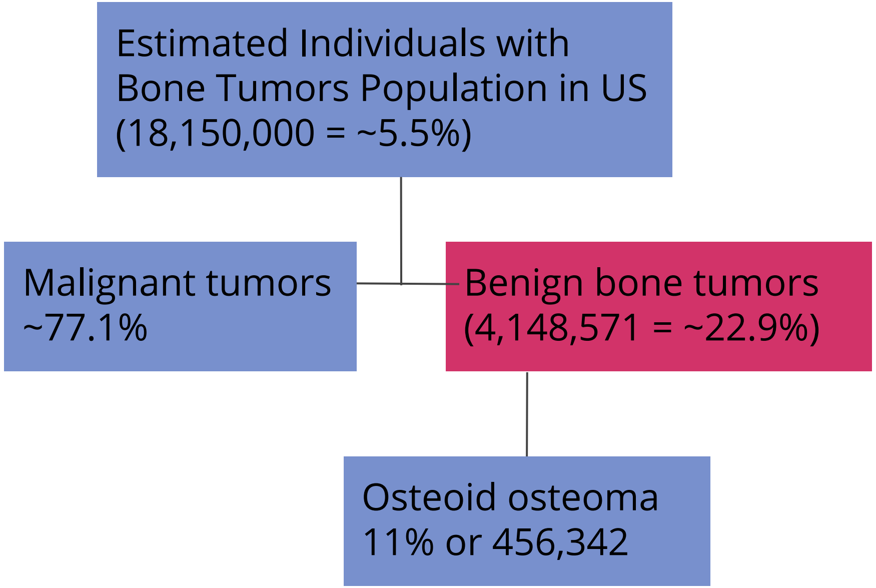
Market Size: ~450,000 * $1,940/patient = $873,000,000

Value Proposition: Lower Ablation Zone and novel application

Product Code: NEY

Regulation Number: 878.4400

Regulatory Pathway: Class 2, 510(k)



G. R. Gaumer, D. S. Weinberg, C. D. Collier, P. J. Getty, and R. W. Liu, "An Osteological Study on the Prevalence of Osteochondromas," *The Iowa orthopaedic journal*, vol. 37, pp. 147–150, 2017, Accessed: Feb. 23, 2021. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5508295/

S. Noordin *et al.*, "Osteoid osteoma: Contemporary management," *Orthopedic Reviews*, vol. 10, no. 3, Sep. 2018, doi: 10.4081/or.2018.7496.

S. A. Astani, M. L. Brown, and K. Steusloff, "Comparison of Procedure Costs of Various Percutaneous Tumor Ablation Modalities," *The Association for Medical Imaging Management,* Aug 2014, Accessed: Feb. 23, 2021. [Online]. Available: http://www.ahra.org/AM/Downloads/OI/qc/RM364_p12-17_Features.pdf

Traceability Matrix

User Needs	Design Inputs	Design Outputs	Design Verification	Design Validation
Temperature Safe Ablation Tip	Temperature of the ablation tip shall not exceed 44 degrees Celsius	Temperature sensor	Temperature Calibration Test	Feedback about temperature monitoring from surgeons, Beta Testing
		Circuit Diagram	Multisim Simulation	
Sterility	Sterility Assurance Level of at least 10^6	Ethylene Oxide Sterilization	Chemical Indicator Sterilization Test	User feedback on temperature needed to store, Ethylene Oxide Fluid Dynamic Modeling
		Sterile Packaging	Seal Testing	
		Packaging Temperature	Tempertaure Indicator on Package	
Efficiency	Must operate between 915 MHz and 2450 MHz	Circuit Design	Multisim Simulation	Ablation time of less than 10 minutes, average of 5 minutes in an ex-vivo study, or in an in-vitro clinical trial.
			Electromagnetic Simulation	
Variability in Pulse	Must be able to deliver 900-1500 V with a sub-nanosecond rise time, dependent on user input, Must have a method for User input (dial, touchscreen, etc.)	Power Supply Datasheet	Benchtop Testing	Test effective ablation on various tumor sizes in-vitro or ex-vivo
		Circuit Design	Multisim Simulation	
		Solidworks part for user control	Assembly Verification	
Biocompatability	Contact between cells and probe shall have >95% cell viability	Materials data sheet for chosen biocompatible metal/polymers	Chemical Testing	In vivo testing proves no adverse immune responses
			MTT assay	

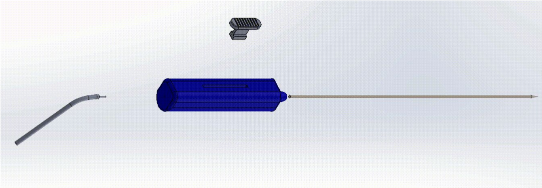
ANSI/AAMI ST67:2003. Sterilization of health care products – Requirements for products labeled "STERILE." This standard requires an SAL value of 10^6 (design input) for products that are intended to come into contact with breached skin or compromised tissue or invasive products that enter normally sterile tissue.

Traceability Matrix (Continued)

User Needs	Design Inputs	Design Outputs	Design Verification	Design Validation	
Usability	Probe shall weigh less than 2 lbs	Materials data sheet [4]	Weight Testing	Test that the probe can be lifted and maneuvered easily by physicians; ask for user feedback from physicians	
		Solidworks Schematic of Probe [3]	Statistical testing with weights of probes of different materials		
Shelf Stable	Probes shall have a shelf life of 4 years from the date of sterilization	Dupont Tyvek Lid Specifications	Seal Testing	Accelerated aging testing (shelf life testing), package strength testing, and package integrity testing according to ISO 11607	**ISO 11607-1:2009. Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems**. This standard outlines material testing methods, packaging systems, and specific requirements to maintain sterility of the device as it is stored until it is ready to be used. These methods and requirements will be used to ensure a shelf life of 4 years (design input) which appears to be the standard shelf life for most thermal ablation probes.
		Materials data sheet [4]	Material Compatability Testing		
Temperature Safe Ablation Shaft	Temperature of shaft should not exceed 41 degrees Celsius.	Temperature sensor	Thermal FEA (Transient)	Ex vivo tests that monitor the temperature of the shaft during ablation for the longest possible ablation duration.	[1] Multisim Simulation [2] Schematic of PCB Design [3] Solidworks Parts and Assembly [4] Data Sheet in Design Outputs
		Saline Cooling System	Temperature Calibration Test		
		Insulation			
Rigidity	The probe tip should withstand 50N of force with no deformation	Materials data sheet [4]	Finite Element Analysis	Feedback from physicians who insert probe into patient's tissue with no deformation.	
		Mechanical Reinforcements	Three Point Bending Test		
			Compression Test		
Comfortable	Probe diameter must not exceed 2mm	Solidworks Schematic of Probe [3]	Assembly Verification	Feedback from patients on any discomfort during and after the procedure due to the diameter	

Solution

- Nanosecond Pulse Electric Field (nsPEF) Ablation
  - High-intensity pulsed electric fields with a nanosecond pulse duration
  - Creates pores in both the plasma membrane and intracellular membrane
    - Induce apoptosis in tumor cells
  - <u>Subnanosecond Pulse Generator</u> - creates pulses of electrical energy
  - <u>Probe</u> - application of electric field to tumor
  - <u>Thumb Tab</u> - control depth of insertion
  - <u>Insulator</u> - protect surrounding tissue

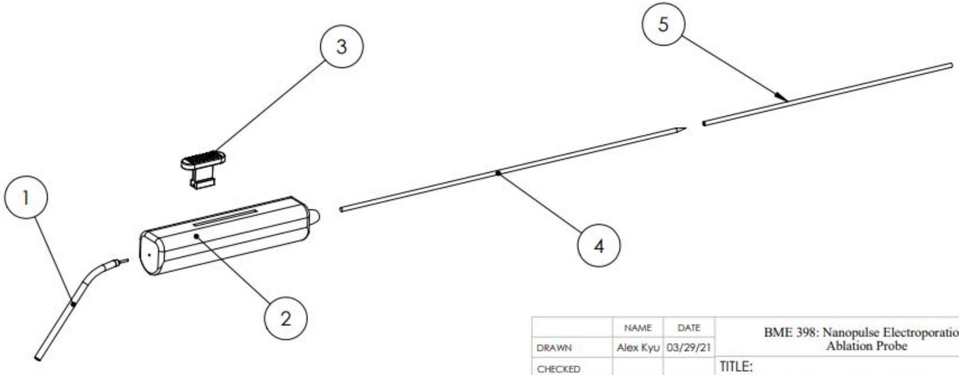


Bill of Materials

Component	**Cost**
PCB Materials*	$ 420.33
Metal Probe	$ 6.99
Thumb Tab	$ 9.99
Handle	$ 9.99
Custom Wire	$ 6.99
Insulator	$ 17.99
Total	$ 472.28

* see Appendix A

ITEM NO.	PART NUMBER	DESCRIPTION	QTY.
1	Probe Wire	Copper Wire between Generator and Probe	1
2	Probe Handle	Polypropylene Handle	1
3	Thumb Tab	Thumb Tab to adjust Exposed Probe Length	1
4	Probe Shaft and Tip	Conductive Shaft	1
5	Insulator	Probe Shaft Insulator	1



	NAME	DATE
DRAWN	Alex Kyu	03/29/21
CHECKED		
ENG APPR.		
MFG APPR.		
Q.A.		
COMMENTS:		

BME 398: Nanopulse Electroporation Ablation Probe

TITLE:

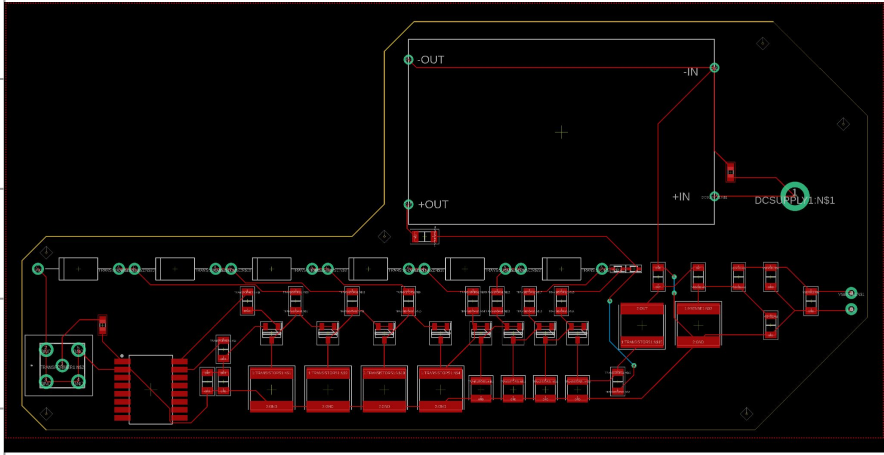
Explosion View and BOM

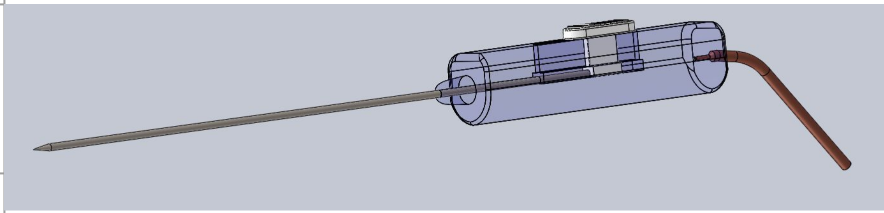
SIZE A | DWG. NO. Full Assembly | REV 1.0

SCALE: 1:2 | WEIGHT: 40 g | SHEET 1 OF 1

Manufacturing Methods

Part	Supplier/Manufacturer	Material
Plastic Handle	Injection Molding	Polypropylene
Insulator	Insulon® Sheaths	Stainless Steel
Probe	Lathe	Stainless Steel
Wire	Y.C. Cable®	Multiple
Thumb Probe Adjustor	Injection Molding	Polypropylene
Generator	JLCPCB®	PCB





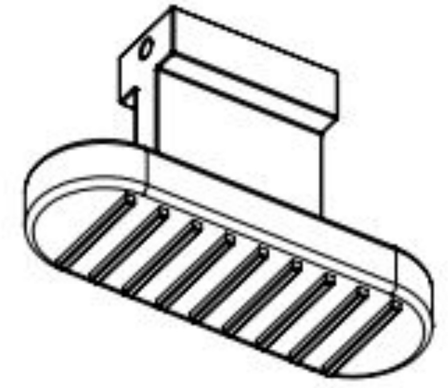
DFM Principles

Principles used in our design:

a. Largest Acceptable Tolerances (outer portion of handle)
b. Available Manufacturing Techniques in the Fab Lab
c. Geometry (Cylinders!)

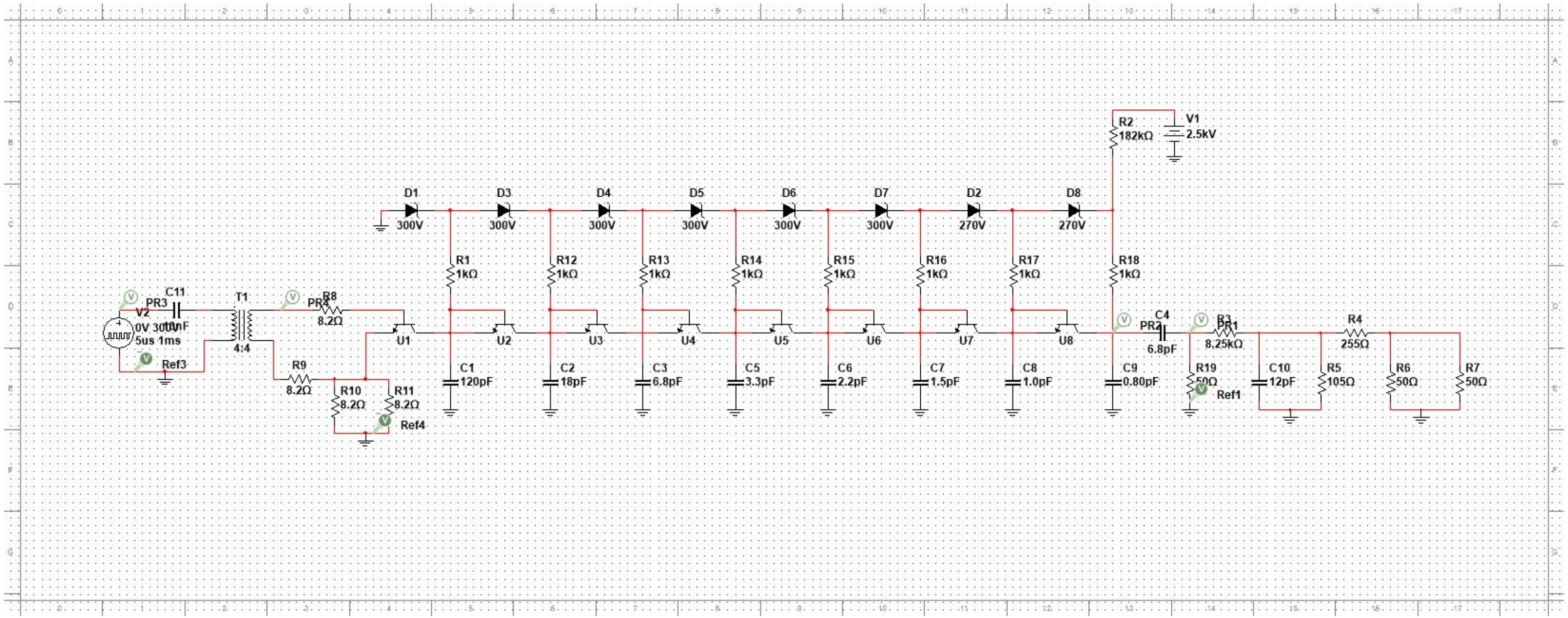
Possible areas of improvement:

a. Poka Yoke (Thumb Tab)
b. Singular Axis of Assembly (Divide handle)



Verification/Validation

Multisim Simulation of Power Generator Circuit



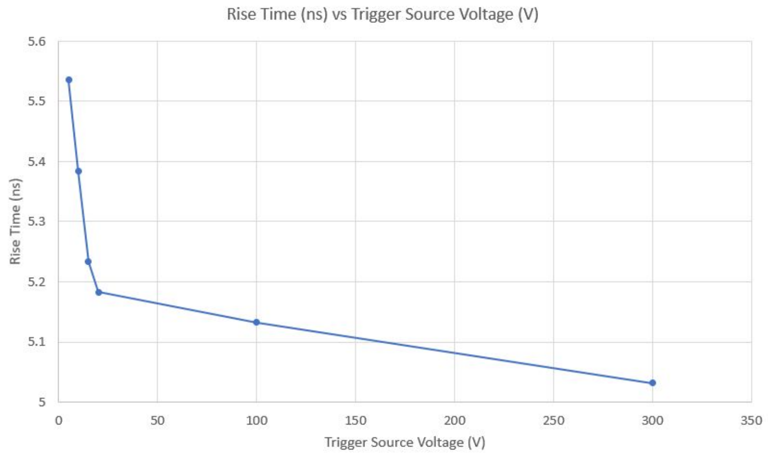
T. Koga, K. Morotomi-Yano, T. Sakugawa, H. Saitoh, and K. Yano, "Nanosecond pulsed electric fields induce extracellular release of chromosomal DNA and histone citrullination in neutrophil-differentiated HL-60 cells," *Scientific Reports*, vol. 9, no. 1, Jun. 2019, doi: 10.1038/s41598-019-44817-9.

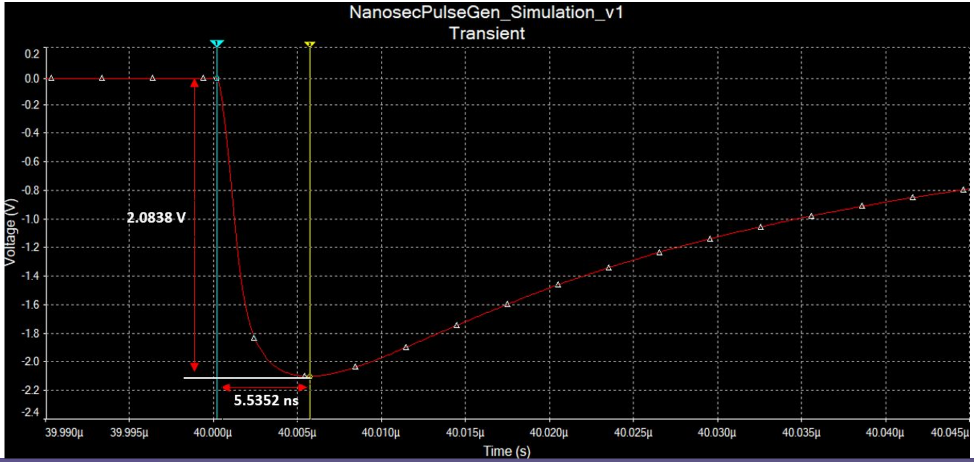
Verification/Validation

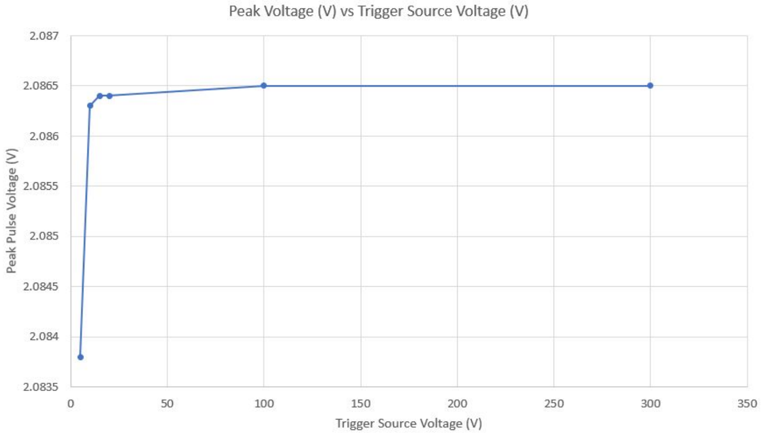
User Need: Variability in Pulse

Design Input: Must be able to produce waveforms of peak voltages between 900-1500 V with a sub-nanosecond rise time

Neither satisfied, accurate spice code for transistor needed







Project Analysis and Future

- Future studies:
  - Prototype generator to analyze output voltage
  - Test the pulse generator with the ablation probe on an ex vivo tissue sample
  - Will likely need to raise additional funds for project (estimated prototype cost $472.28)
  - Timeline is achievable, although will be tight
- Risks
  - Overall Success
    - Generator not producing desired output waveform
    - Financial Risk: expensive prototype
  - User Harms
    - Leakage Current
    - Electric Field produced too large
    - Detached thumb tab
    - Misinterpretation of user interface to set ablation power
- Continuing For Senior Design
  - Solution meets unmet clinical need with a large market size
  - Design is feasible to manufacture, especially using Fab Lab

Questions?

Appendix A - Full PCB BOM

Part Name	Unique Identifying Number	Description	Quantity	Material	Vendor	Unit Cost	Total Cost
Avalanche Transistor	TR1	Avalanche Transistor	8	n/a	Mouser	$9.73	$77.84
DC-DC Converter	CONV1	DC-DC Converter	1	n/a	PicoElectronics	$136.24	$136.24
Resistors (1K)	R1	Resistors (1K)	8	n/a	Mouser	$1.25	$10.00
Resistors (8)	R2	Resistors (8)	4	n/a	Mouser	$0.46	$1.84
Resistors (181K)	R3	Resistors (181K)	1	n/a	Mouser	$0.10	$0.10
Resistors (50)	R4	Resistors (50)	1	n/a	Mouser	$1.62	$1.62
Resistors (8.5k)	R5	Resistors (8.5k)	1	n/a	Mouser	$0.10	$0.10
Resistors (255)	R6	Resistors (255)	1	n/a	Mouser	$0.10	$0.10
Resistors (105)	R7	Resistors (105)	1	n/a	Mouser	$0.10	$0.10
Capacitor (120p)	C1	Capacitor (120p)	1	n/a	Digikey	$21.32	$21.32
Capacitor (18p)	C2	Capacitor (18p)	1	n/a	Digikey	$14.34	$14.34
Capacitor (6.8p)	C3	Capacitor (6.8p)	2	n/a	Digikey	$14.34	$28.68
Capacitor (3.3p)	C4	Capacitor (3.3p)	1	n/a	Digikey	$15.50	$15.50
Capacitor (2.2p)	C5	Capacitor (2.2p)	1	n/a	Digikey	$1.50	$1.50
Capacitor (1.5p)	C6	Capacitor (1.5p)	1	n/a	Digikey	$1.50	$1.50
Capacitor (1.0p)	C7	Capacitor (1.0p)	1	n/a	Digikey	$1.50	$1.50
Capacitor (0.8p)	C8	Capacitor (0.8p)	1	n/a	Digikey	$0.80	$0.80
Capacitor (12p)	C9	Capacitor (12p)	1	n/a	Digikey	$14.34	$14.34
Capacitor (0.1u)	C10	Capacitor (0.1u)	1	n/a	Sparkfun	$0.95	$0.95
Capacitor (10n/0.01u)	C11	Capacitor (10n/0.01u)	1	n/a	Sparkfun	$0.95	$0.95
Zener Diode (300 V)	D1	Zener Diode (300 V)	6	n/a	Mouser	$12.67	$76.02
Zener Diode (270 V)	D2	Zener Diode (270 V)	2	n/a	Mouser	$0.30	$0.60
SMA Connector	J1	SMA Connector	1	n/a	Mouser	$3.07	$3.07
Transformer	T1	Transformer	1	n/a	Digikey	$3.92	$3.92
PCB	PCB1	Printed Circuit Board	1	n/a	JLCPCB	$7.40	$7.40
						Total	$420.33