µTissue Dicer

Fall Quarter Final Presentation

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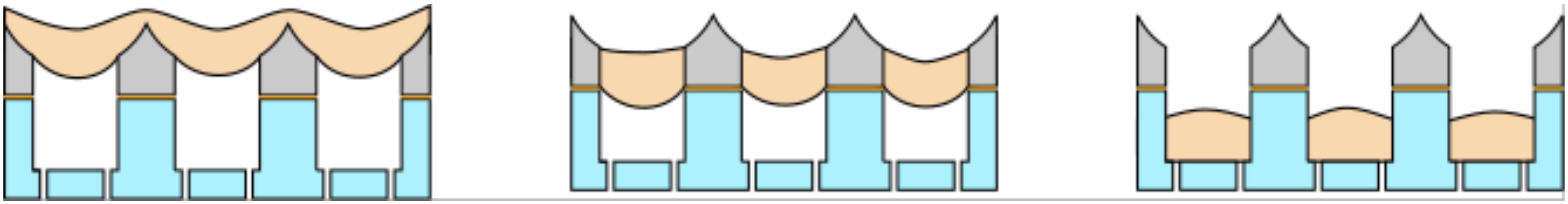
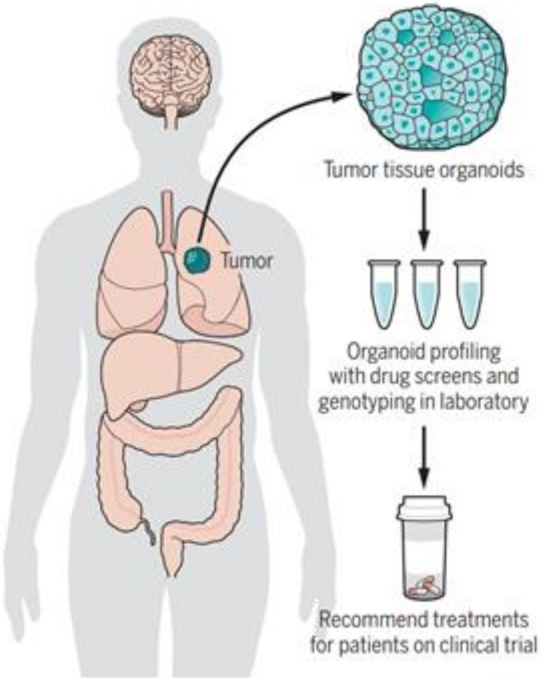


Motivation

- No current methods for generating high-throughput, uniform fragments of organoids that reflect spatial heterogeneity of original cancer tissue
- Our device will be critical to study organoid fragments that preserve tumor microenvironments (TME) and resident immune cells
- Improve throughput of multiplexed drug screening to support personalized cancer immunotherapy treatments

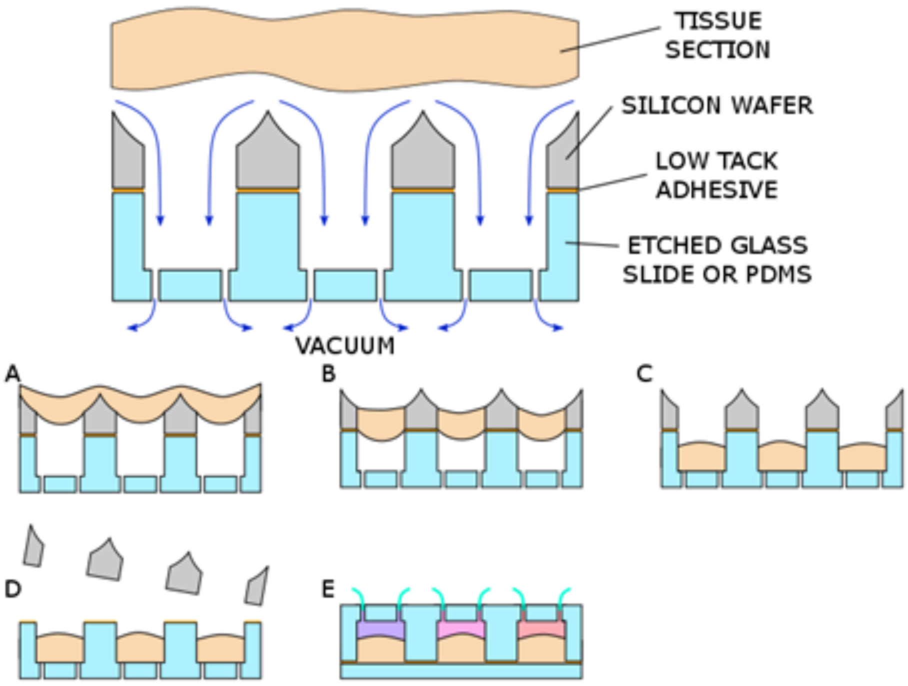


For the SNF:

- Expanding operational and functional utility of PT-DSE for non-conventional silicon etching
- Optimizing SOP for large feature etching (i.e. deep and wide)

Top: multiplexed cancer drug screening microfluidic assay based on culturing cancer cells (not organoids) (Zhang et al., *Small,* 2018). **Left:** target etch features represent fabricated by unique plasma etching recipes

Concept



Cross-sectional schematic

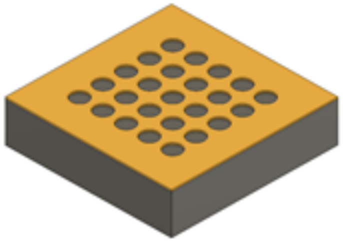
(A-C) Extrude tissue through etched silicon blade into microwells

(D) Remove blade array

(E) Interface with microfluidic network for individually addressable wells

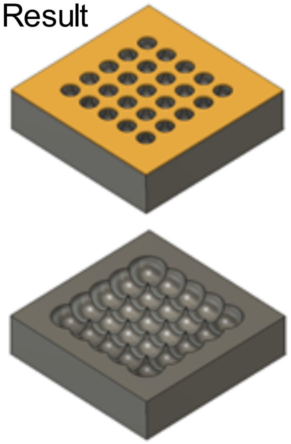
Fabrication Method

Step 1: Pattern photoresist mask on Si wafer using Heidelberg

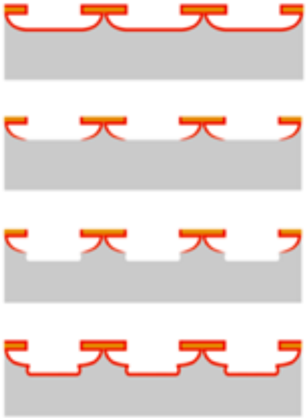



Step 2: Pseudo-isotropic etch with PT-DSE to create blades.

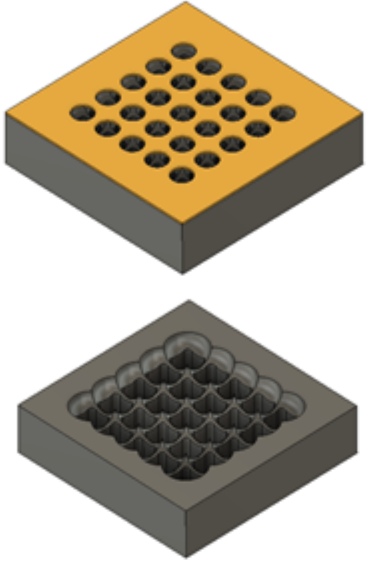
Etch Result



Step 3: DRIE etch vertical trenches down to ~50 µm using Bosch process.

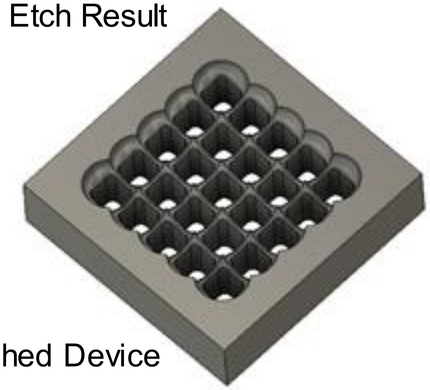


Etch Result



Step 4: KOH etch backside to expose through-holes

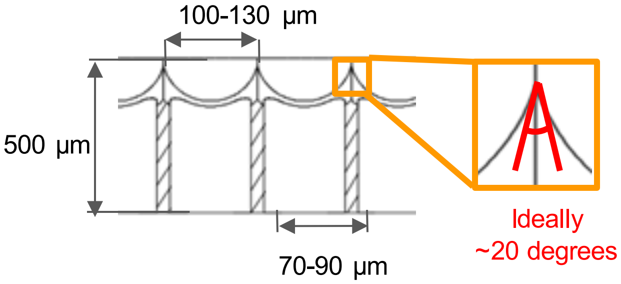
Etch Result



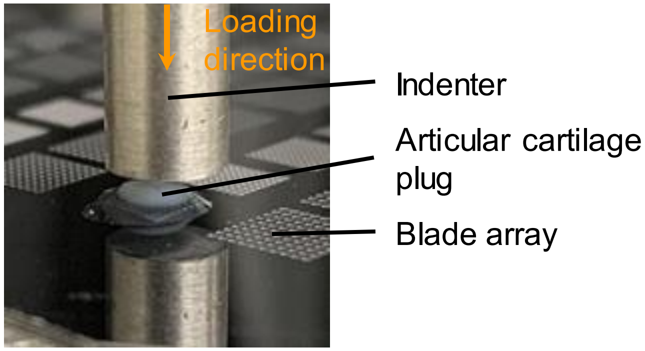
Finished Device

Objectives

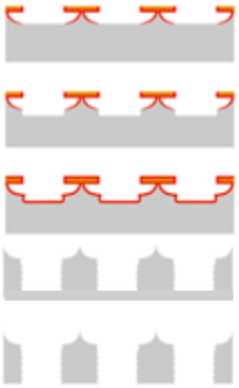
Objective 1: Optimize etch recipe for blade angle by tuning gas ratio to develop profile that is not crystal plane dependant (pseudo-isotropic).



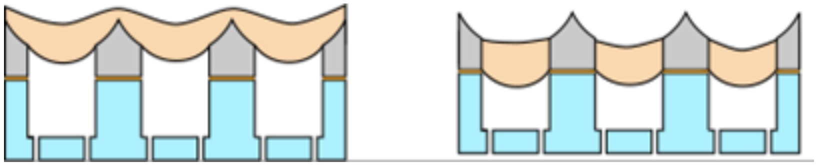
Objective 2: Test etched devices against tissue phantom with compression test to validate cutting ability.



Objective 3: Etch through-holes in wafer and strengthen cutting surface by passivation with platinum.



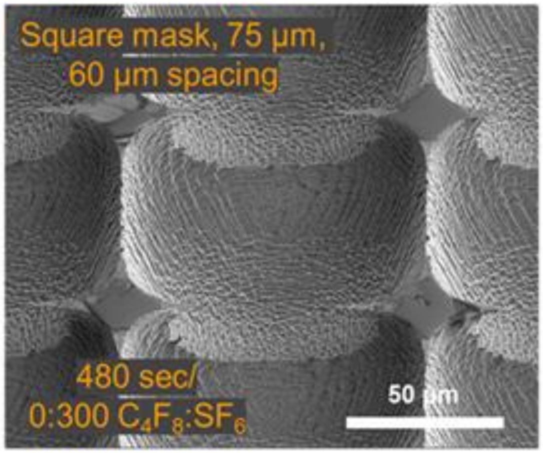
Objective 4: Couple with extruding force to draw tissue through the device into collection microwells.

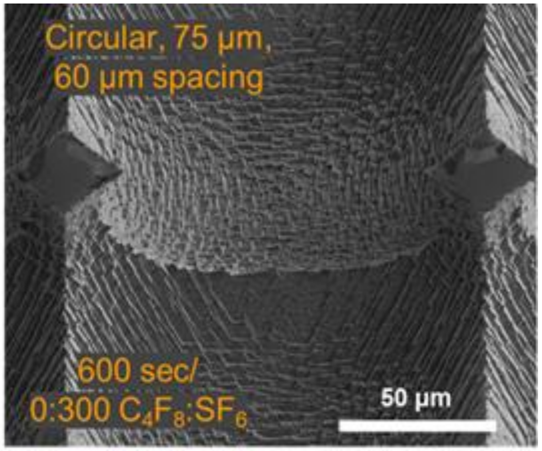


Results (towards blade array etching)

Increasing SF_6 Time

Increasing C_4F_8 in process module



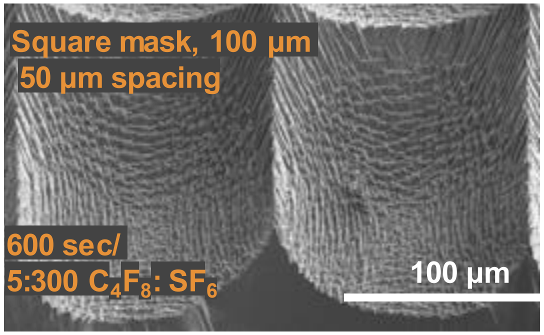


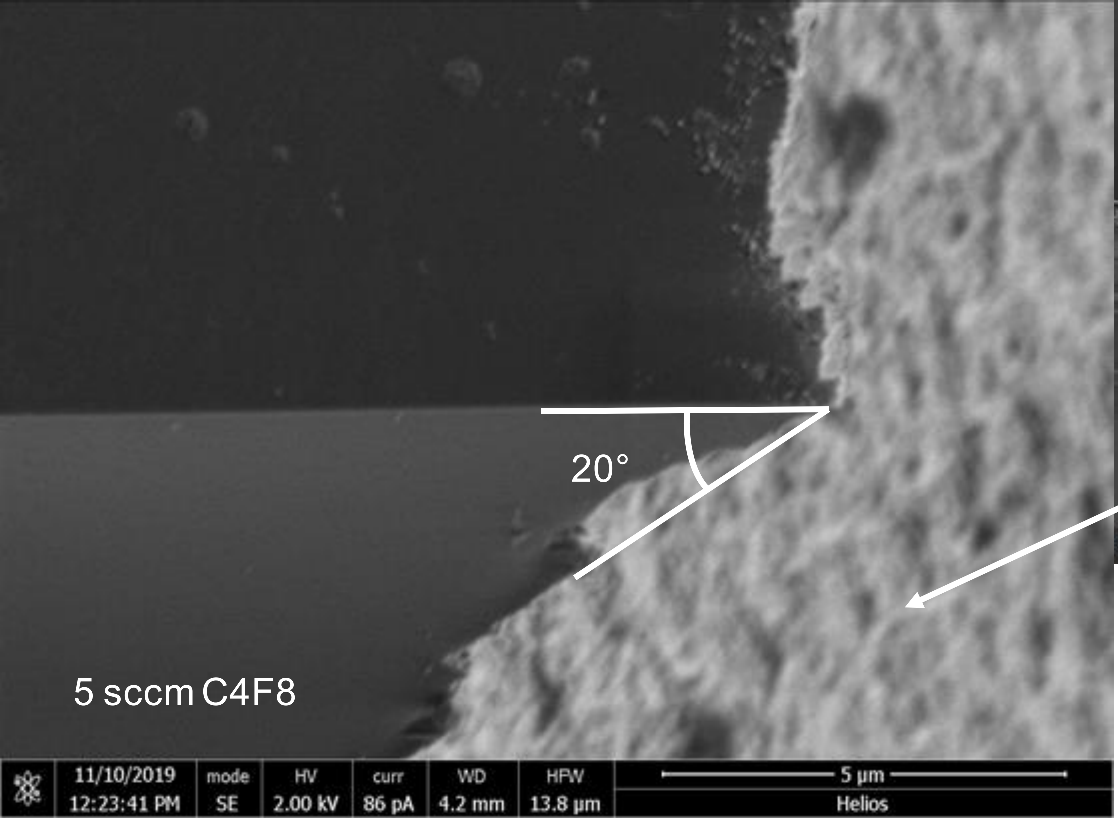
Bosh Process: Plasma etching with SF_6 and C_4F_8. No passivation or cycling.

Parameters:

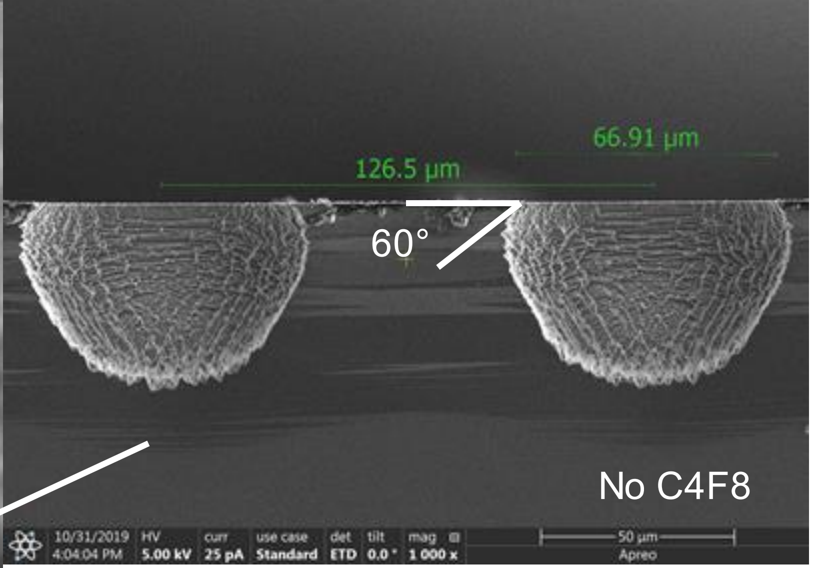
1) Ratio of C_4F_8: SF_6 determines the blade angle
2) Time SF_6 added determines depth of isotropic etching

Photoresist Selectivity: **~250: 1**

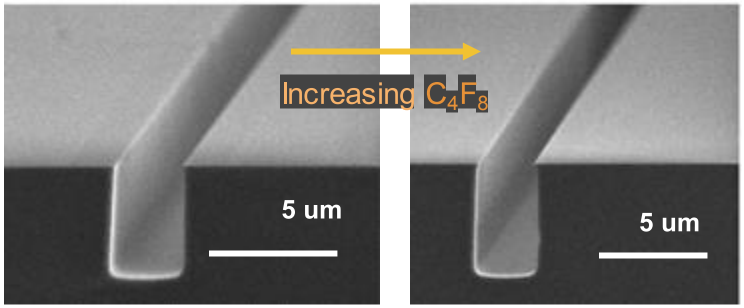




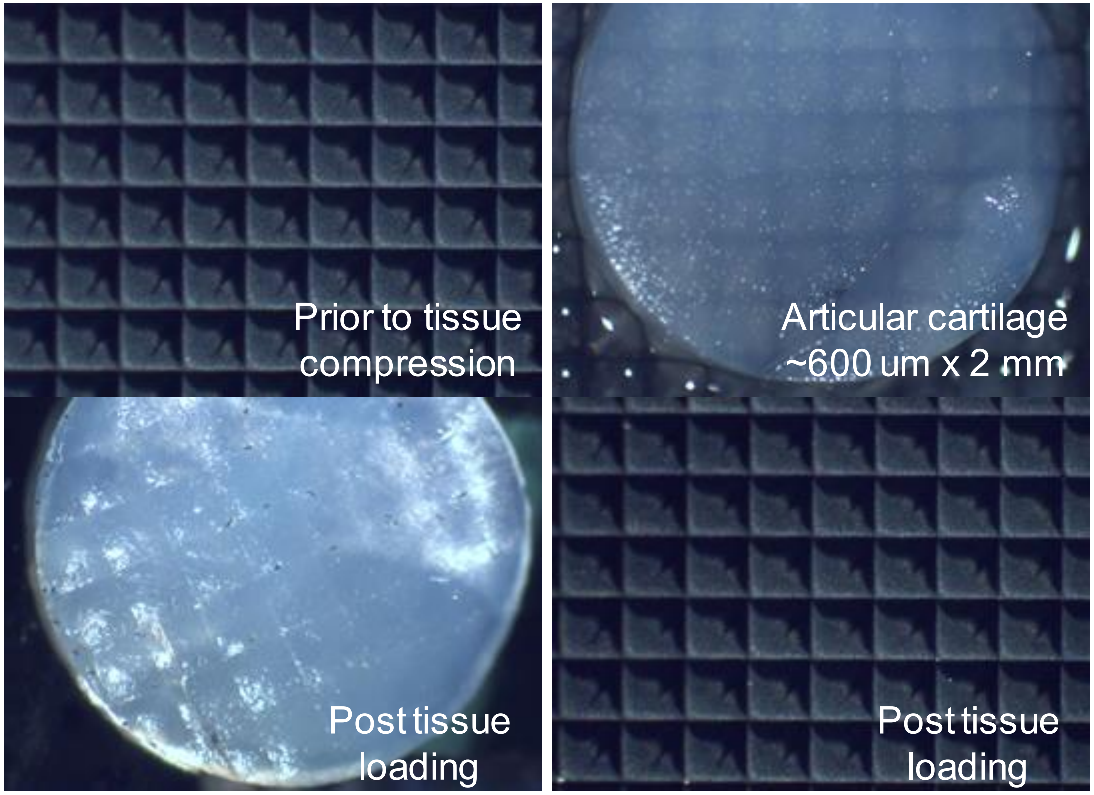
Jagged edges are a result of fluoropolymer formation (fluorine radicals + photoresist polymer). We will further characterize the undercut angle and blade sharpness in the next quarter with an oxide mask.

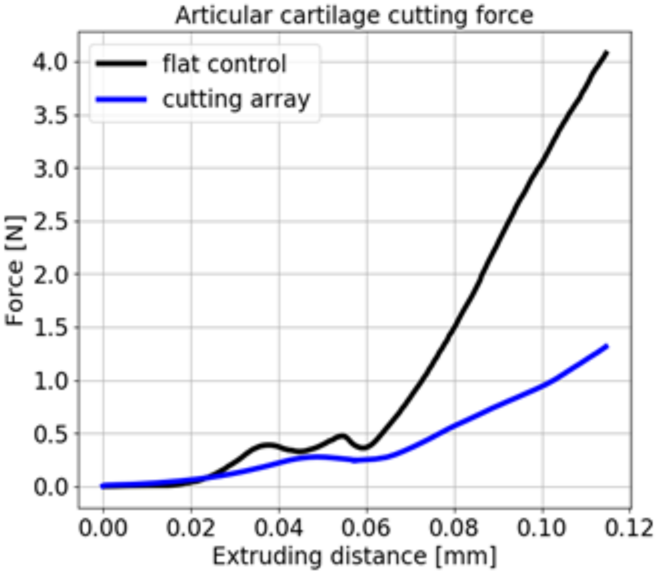


Increasing C4F8 appears to decrease the undercut angle. Results are consistent with previous characterization of Bosch process: (SEMs below courtesy of Settasit C.)



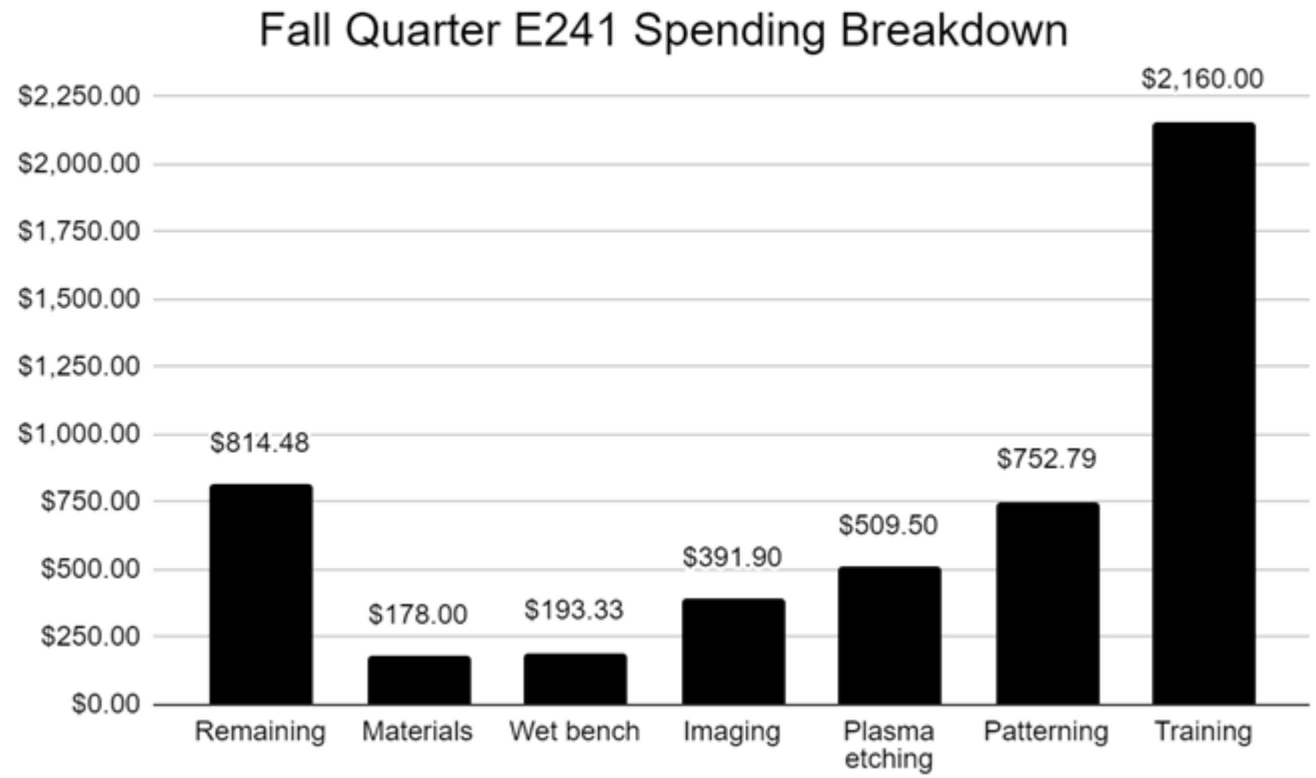
Results (preliminary mechanical testing)





- Loaded at 0.02 mm/s in buffer
- Evidence of cutting seen in flatter loading profile on cut sample, i.e. plateauing force is indicative of slipping or cutting in this case.

Budget



- Wet bench:
  - Wbflexcorr
- Imaging:
  - SEM (thank you David!)
  - Keyence
- Plasma etching:
  - PT-DSE
  - Oxford-RIE
  - Matrix
- Patterning:
  - CCP-dep
  - YES oven
  - SVG coater/developer
  - Heidelberg
- Training:
  - General safety
  - All-litho
  - Heidelberg
  - Keyence
  - SVG coater/developer
  - Thermco4
  - Matrix
  - Apreo SEM
  - Oxford-RIE
  - Wbflexcorr

Winter Quarter Goals

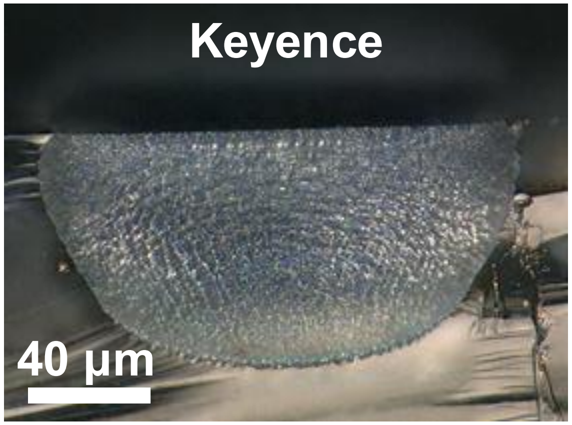
1. Complete Objective 1: Perform pseudo-isotropic etches to form cutting edge using *oxide masked* silicon wafers instead of photoresist.
    a. Characterize how C_4F_8: SF_6 ratio and time affect etch profile in silicon

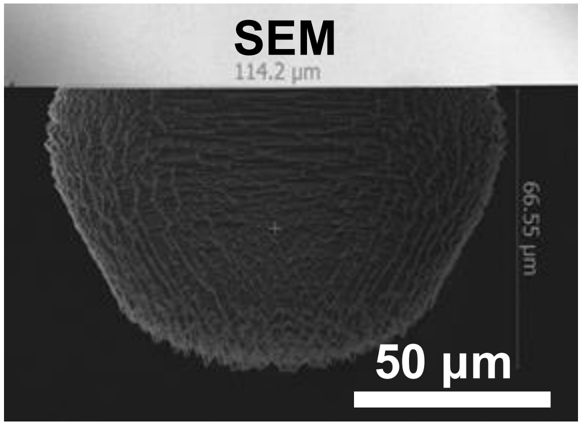
1. Objective 3: Etch through-holes and determine effectiveness of single mask method for etching device and adjust process as needed.

1. Objective 2/4: Pair device with microwell plate (fabricated in PDMS) and test the effectiveness of using a vacuum dessicator or other force to extrude tissue into compartments.

Thank you!
Questions?

Insights: Keyence for profile imaging (Supplementing SEM)





- Keyence digital microscope images of cleaved wafers offer a rapid, cheap alternative to SEM for first pass imaging.

Ox-RIE: Etching oxide using PR as a mask

Recipe:

Start Pump Step: Pump 5e-5

Etch Step: 30 Ar/ **15 CHF3/ 45 CF4/** 100 mT/ 500W/ 20C/ 10T He (5 min etch) **adapted from K.L/ Y.C 2016

End Pump Step: Pump 7e-5

- **Patterned oxide wafer #1:** SCS wafer with 1 um thermal oxide, patterned with 1.6 um 3612 photoresist and resolution mask pattern
    - Measured film thickness with the NanoSpec. Focused/measured in four distinct spots on wafer
    - PR pre-etch thickness: 15,975Å. PR post-etch thickness: 10,283Å.
        - PR Etch rate: 1138 Å / min (*higher than average etch rate reported from K.L/Y.C: note procedure differences)
    - Oxide pre-etch thickness: ~10,000 Å. Oxide post-thickness: Etched all the way (< 100 Å).

- **Patterned oxide wafer #2:** SCS wafer with 1um thermal oxide, patterned with 1.0 um 3612 photoresist
    - Measured film thickness with the NanoSpec.
    - PR post-etch thickness: 142 Å (reported by positive resist on oxide option)
        - Question: Which NanoSpec option is most accurate post-etch?
    - Oxide pre-etch thickness: ~10,000 Å. Oxide post-thickness: Etched all the way (< 100 Å).

4003.47	**TOTAL EXPENSES**	**996.53**	**REMAINING BUDGET**		
Training	Quantity	# Trainees	Cost	Total	
General Safety	1	2	80	$160	
All-Litho	2	3	80	$480	
PTDSE	1.5	3	80	$360	
Heidelberg	2	1	80	$160	
Keyence Digitial	1	2	80	$160	
SVG Coater/ Developer	1	3	40	$120	
Thermco4	0.5	1	40	$20	
Matrix	0	1	0	$0	
SEM + Wetbench+ Oxford RIE				$1220	
				$2680	**TOTAL**
Materials					
Clean Room Notebook	1		8	$8	
Wafer - C-test (100 mm)	6		17	$102	
Cassette (storage) - 100 mm	1		17	$17	
				$127	**TOTAL**

Tool usage	**Amount**	**Cost**	**Date**
Heidelberg	67	$39.08	10/23
SVG coater	88	$73.33	10/23
SVG dev	13	$10.83	10/23
Yes oven	34	$28.33	10/23
SEM	60	$75	10/26
PTDSE	277	$230	10/25
Yes oven	27	$22.5	10/27
SVG coater	16	$13.33	10/28
SVG dev	20	$16.67	10/28
Heidelberg	51	$29.75	10/28
Keyence	118	$68.83	10/28
Keyence	63	36.75	10/29
Yes oven	24	20	10/31
SVG coater	14	11.67	10/31
SVG dev	15	12.5	10/31
Heidelberg	55	32.08	11/1
Keyence	74	43.17	11/3
SEM	45	56.25	11/3
PTDSE	93	77.5	11/3
Matrix	13	10.83	11/3**
Keyence	56	32.67	11/12

1145.47.8	**TOTAL**

Spreadsheet with additional tool usage documented. Budget on this slide **is** up to date: https://docs.google.com/spreadsheets/d/19MMgB_ddmSj47bU34jJghtU5mj3nu56hdJgn2093RMU/edit#gid=0