

# Take a Breath! Managing Breathing Problems after Transplant

Celebrating a Second Chance at Life  
Survivorship Symposium

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# Take a Breath! Lung GVHD and Managing Breathing Problems after Transplant

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*“We are all working so hard to be self-fulfilled, individually successful, and personally healthy...that we have forgotten the real purpose and path to health and healing is to make joyful connections.”*

*- Francis Peabody MD, 1927*

# Quotes from Patients with Breathing Problems after Transplant

“I need to breathe to live, but I also need to live to breathe.”

“I’m alive, but I’ve had so much loss.”

“If I had known I would get lung disease like this, I would have rather died from my AML.”

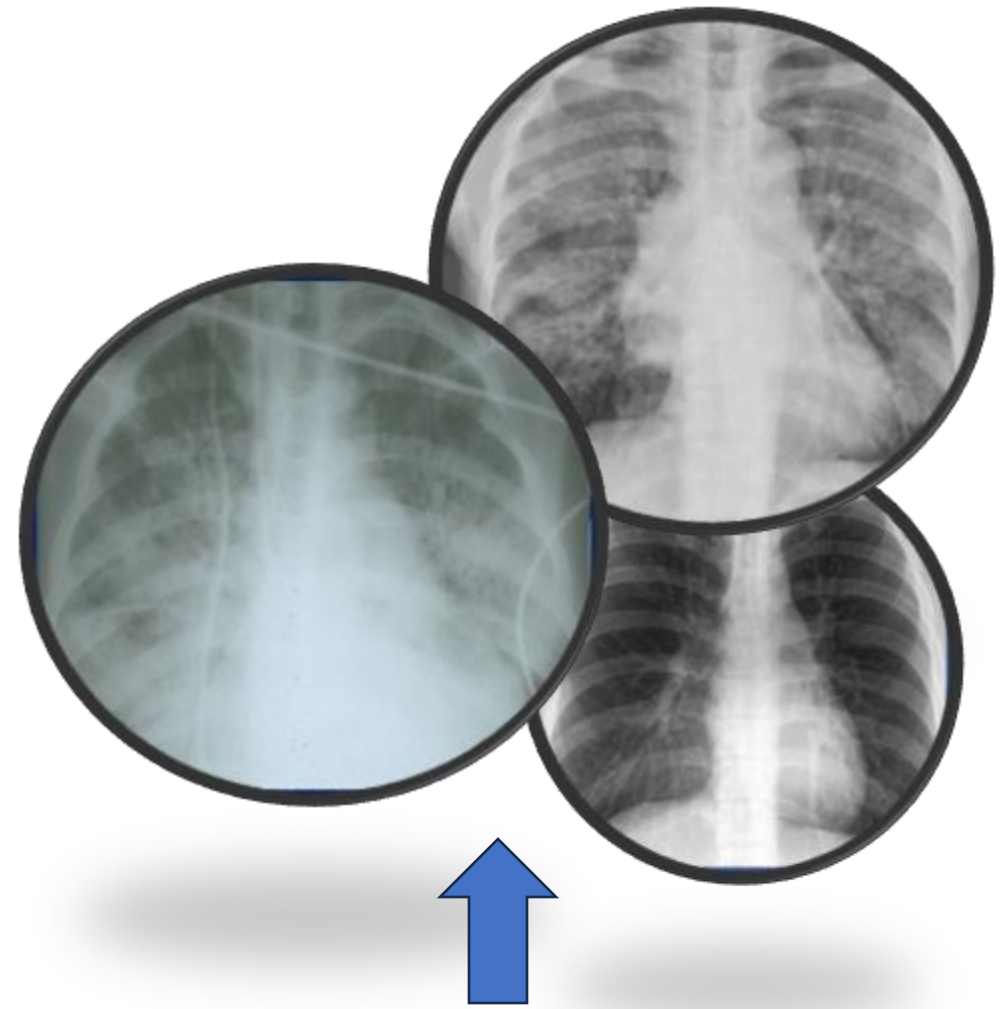
*Courtesy of Guang-Shing Cheng MD  
Fred Hutchinson Cancer Center*

# Pneumonia, Lung Disease and Transplant

- Over 50% of patients will develop pneumonia at some point after transplant. The pneumonia can occur at any time, whether in the first few months, or many years after transplant.
- Not all pneumonias are due to an infection. Many aren't infectious at all.
- By definition, pneumonia simply means that there is “inflammation” in the lungs. For example, fluid, swelling, or irritation to lung tissue can all be present in the lungs, without having an actual infection present.
- In reality though, the lines between infectious and non-infectious pneumonia are often blurred.

# Blurring of the lines

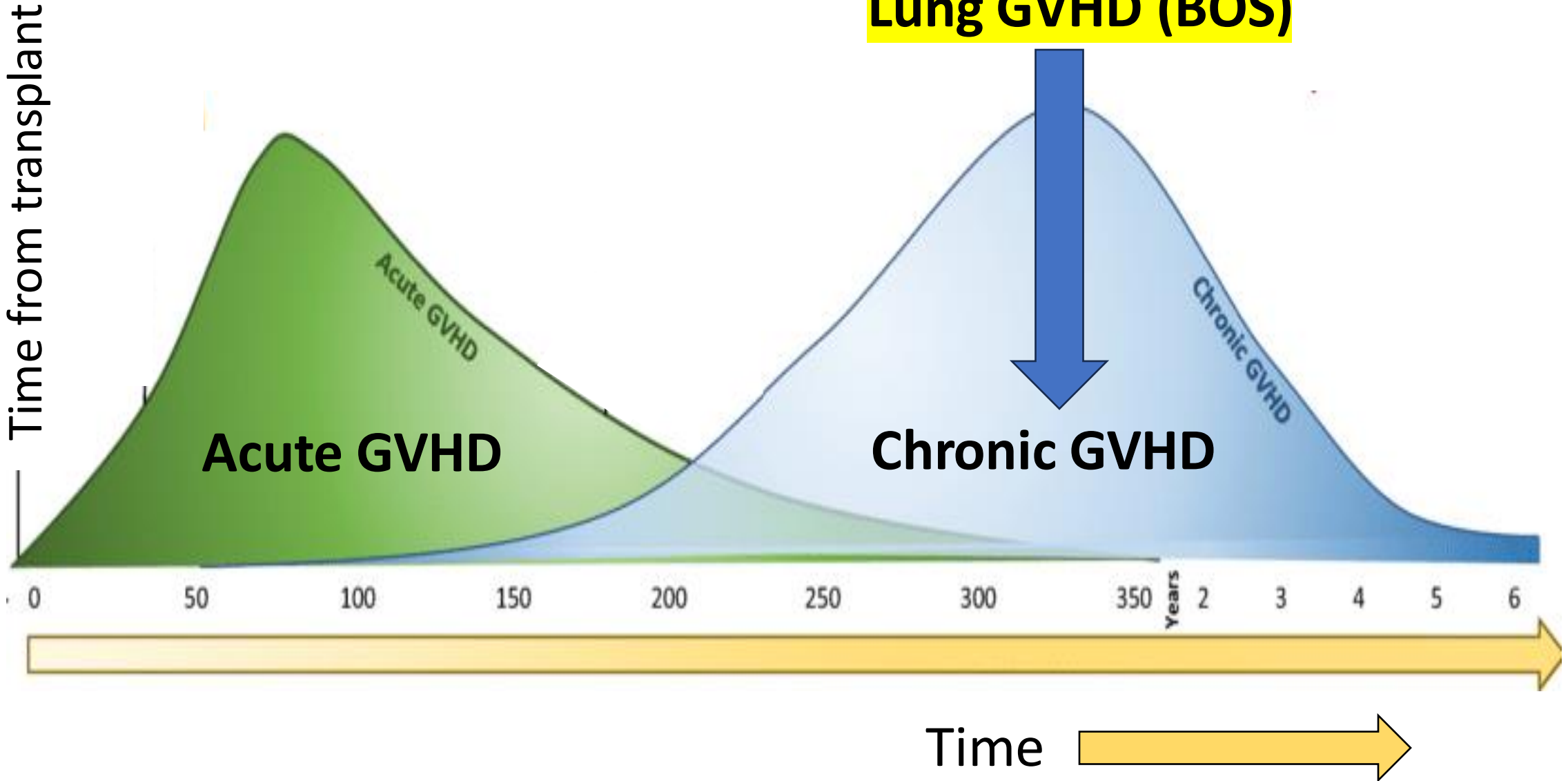
- Infectious pneumonia may often lead to a non-Infectious pneumonia.
- Patients with non-infectious pneumonia are often chronically infected.
- We can't even tell which it is, by looking at a Chest Xray or CT scan.
- Ughh....
- We can start by defining Lung GVH. What is it? How do we test for it? How do we treat it?



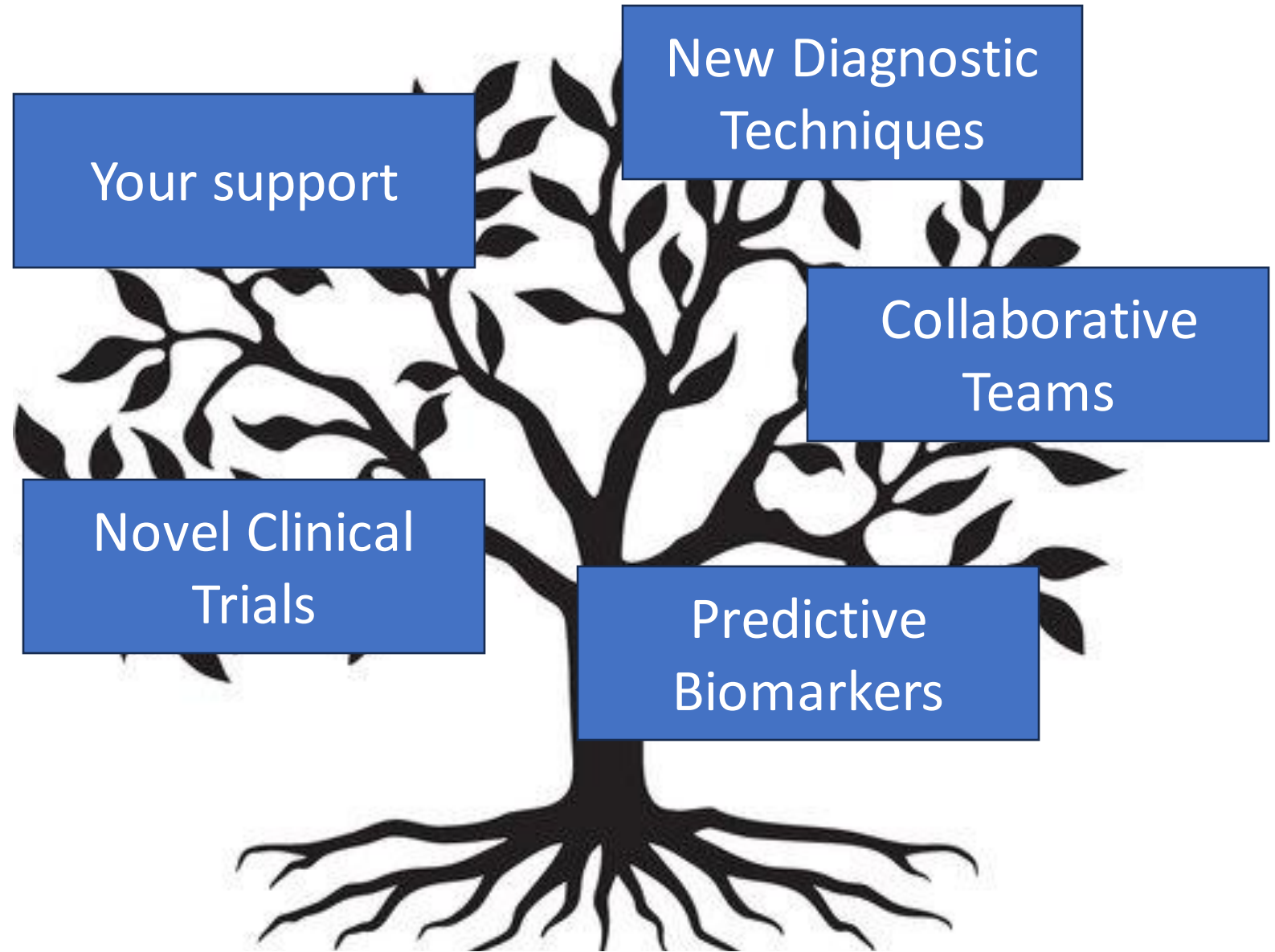
If you asked transplant physicians to look at these chest Xrays and tell you which patients had an infection in their lungs, they couldn't tell you, at least with any accuracy.

# What is Lung GVHD?

- It is a form of chronic graft versus host disease (GVHD).
- An “obstructive” airway disease that occurs ~ 1-year post-transplant. Air can get in. It can't get back out. The air you breathe gets trapped, then stagnant in your lungs. Chronic infections (infectious pneumonia) often occur.
- Symptoms: Shortness of breath, chronic cough.
- Develops in 10-20% of all patients with chronic GVHD
- Medical term: Bronchiolitis Obliterans Syndrome (BOS)



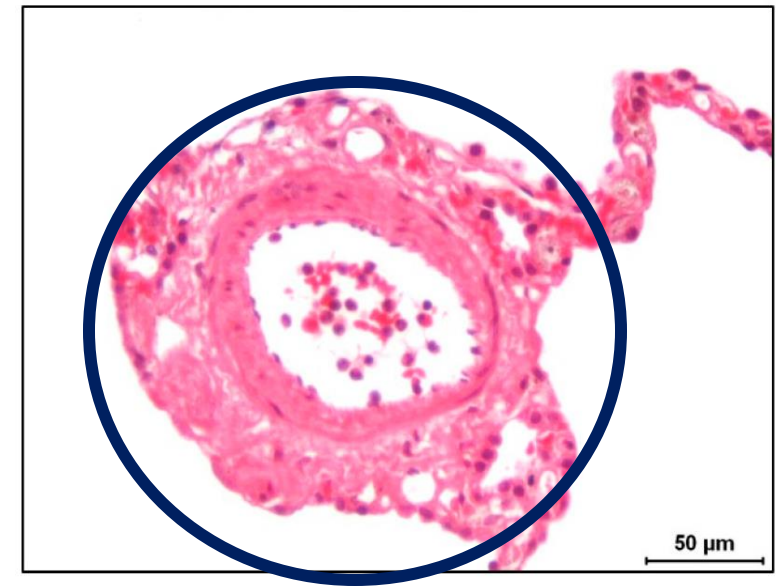
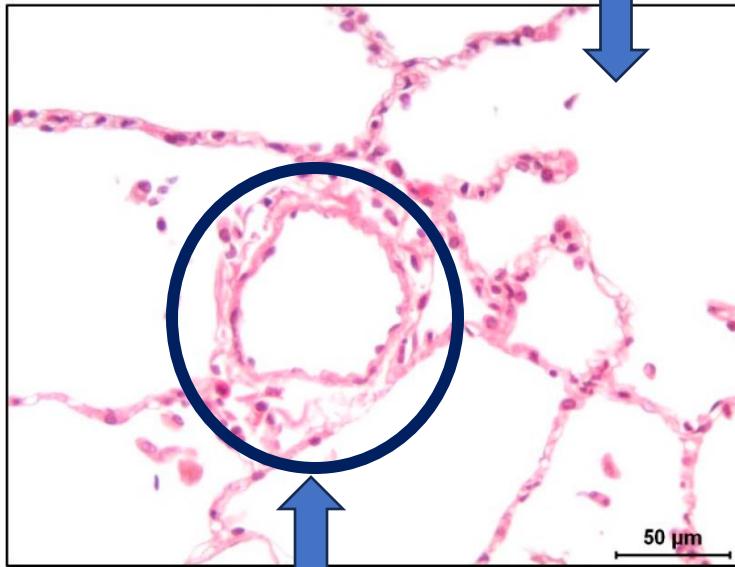
Lung GVHD:  
Over the past  
decade





# Primer: Pathology of Lung GVHD

Air Sac (Alveolus)



Small Airway (Bronchiole)

Normal lungs



Lung GVHD

(Bronchiolitis Obliterans Syndrome)

# Risk Factors for Lung GVHD.

University of Michigan Data Base (n=1016 patients)

Patients at highest risk for developing Lung GVHD:

- Patients with a history of severe acute Graft Versus Host Disease.
- Patients who developed viral infections and/or Pneumonia within the first 100 days post-transplant.
- Patients with low lung function prior to transplant. Measured by a test called Pulmonary Function Testing (PFT).



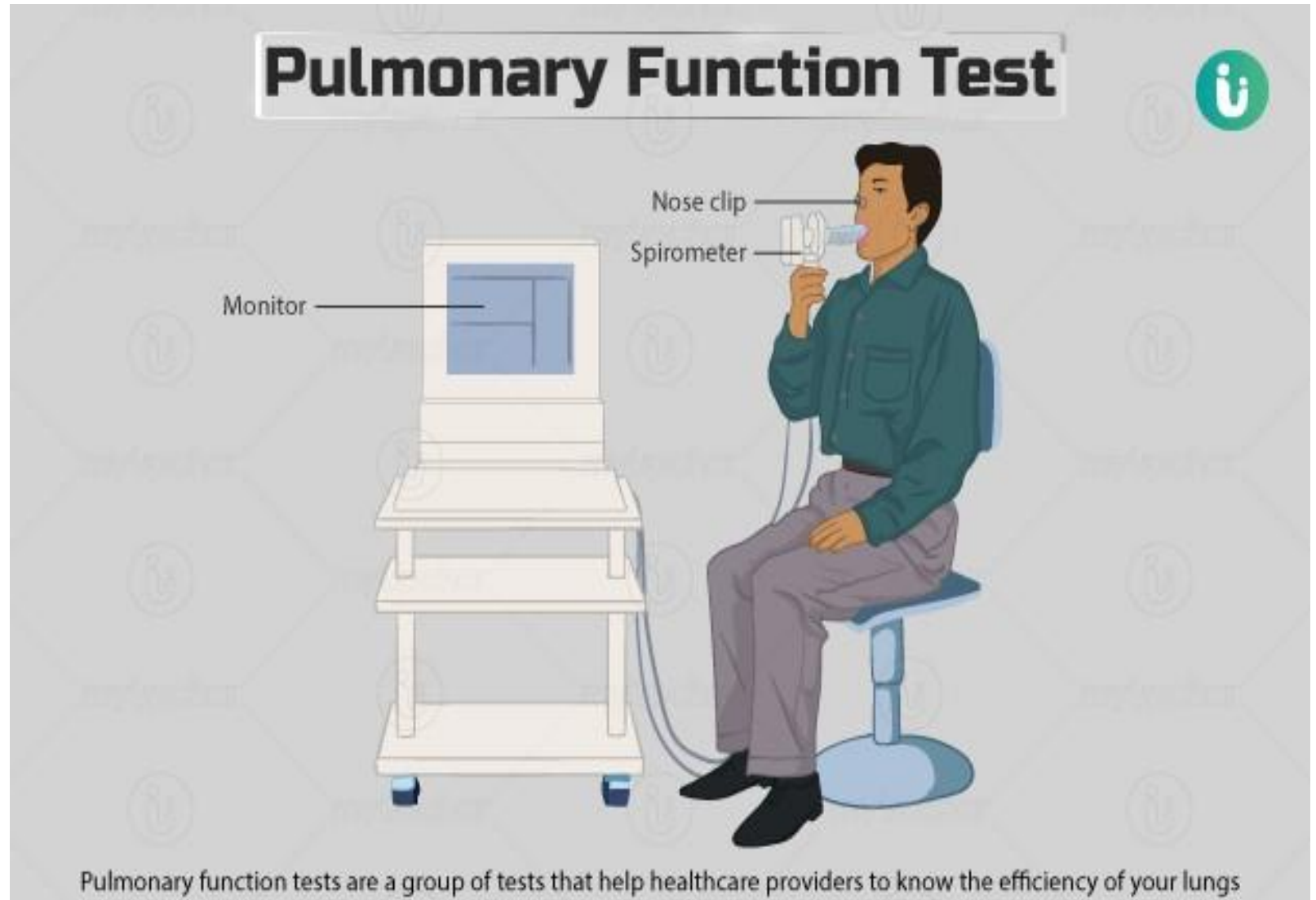
# How is Lung GVHD Diagnosed?

# NIH Criteria for Diagnosing Lung GVHD<sup>1,2</sup>

- **Requires Pulmonary Function Testing (PFT).**
- The main criteria is an FEV1 < 75% predicted for age and size.
- The FEV1 must have declined  $\geq 10\%$  from prior measurements.
- **What does all this mean, in English?**

. Filipovich AH BBMT 2005, 2. Jagasia M BBMT 2015

# Pulmonary Function Testing: Primer

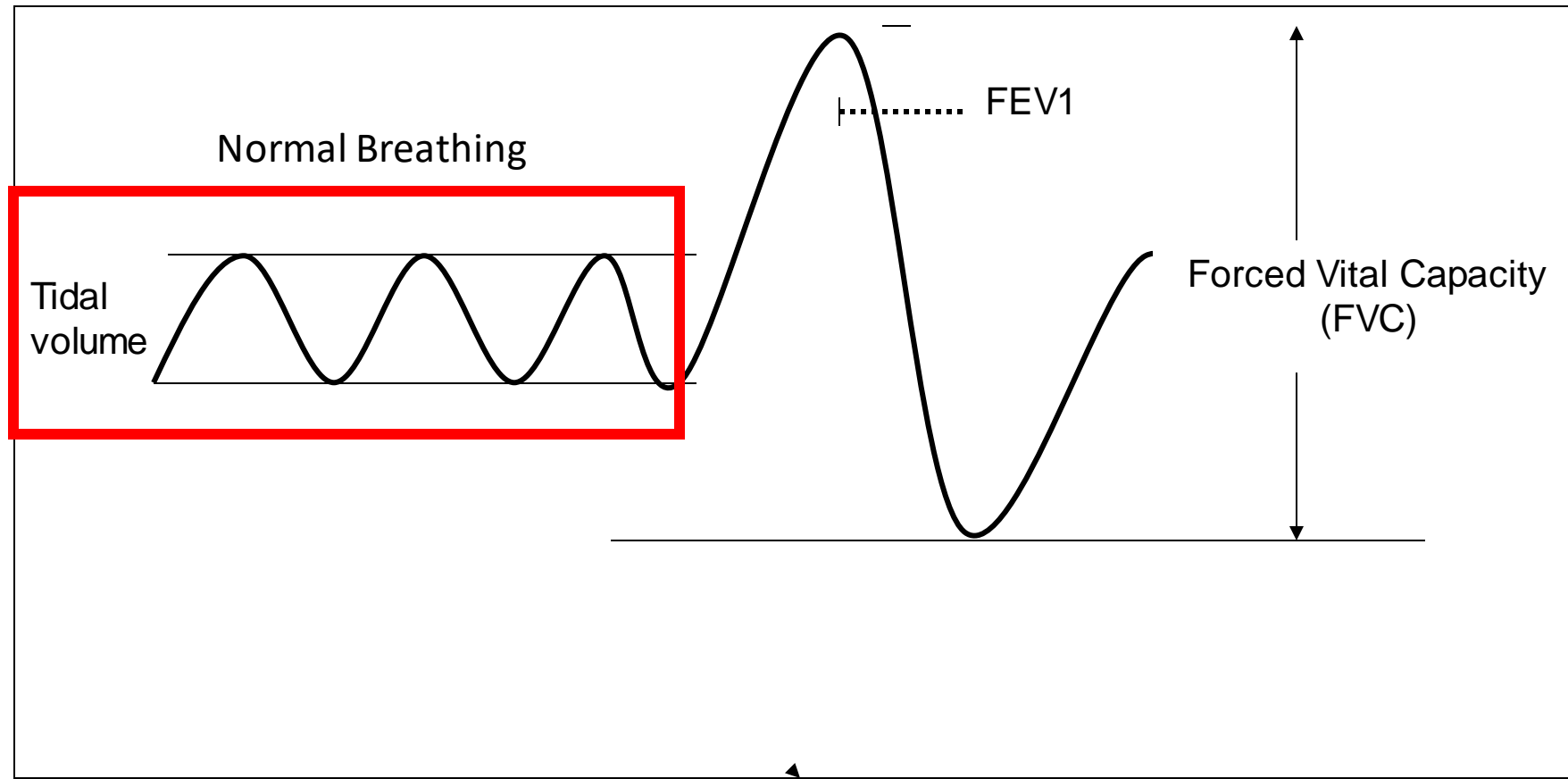


**PFT's: The main parameter we (MD) look at:**

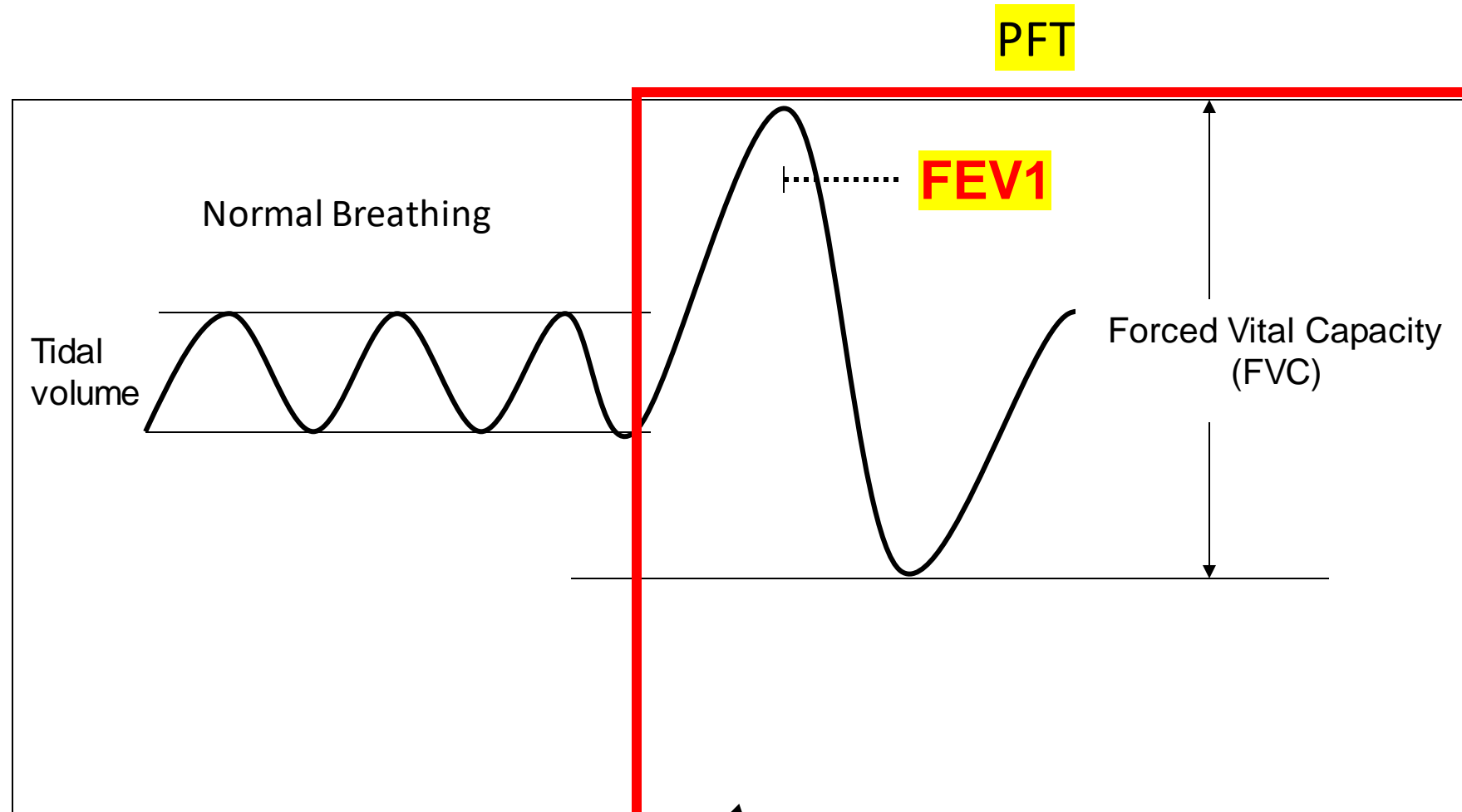
**FEV1: Forced Expiratory Volume in 1 second**

The volume of air you can forcibly exhale in 1 second

# Pulmonary Function Tests: Primer



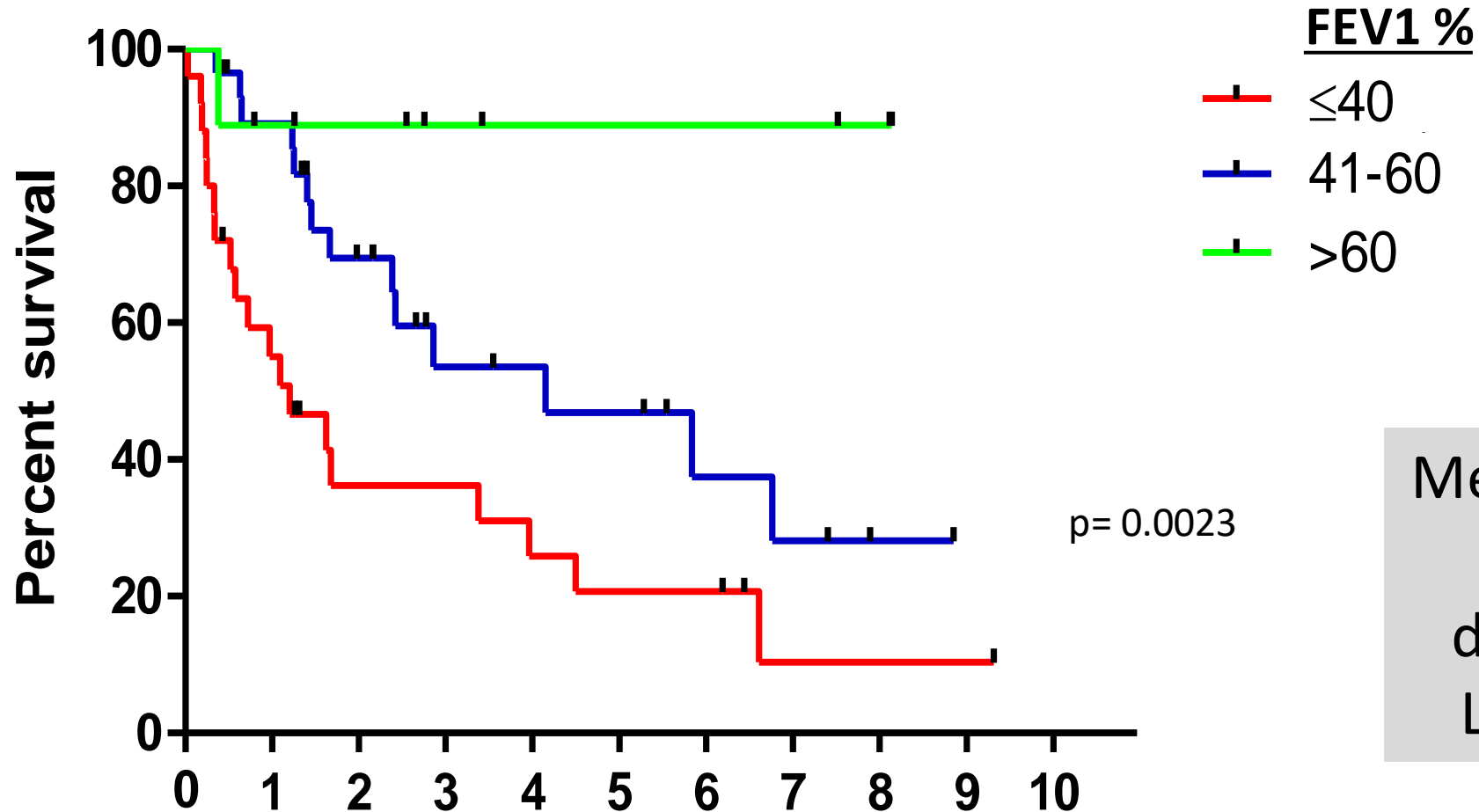
# Pulmonary Function Tests: Primer





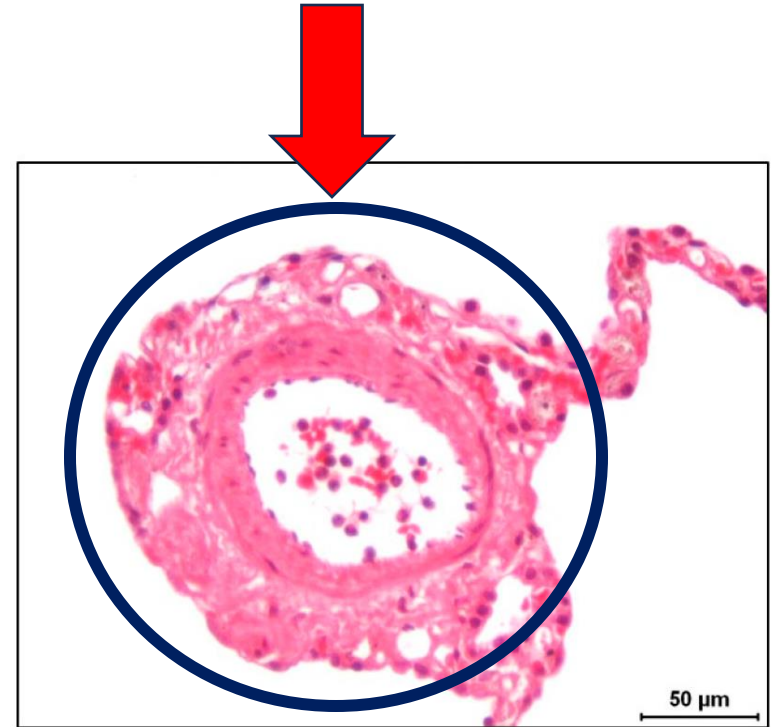
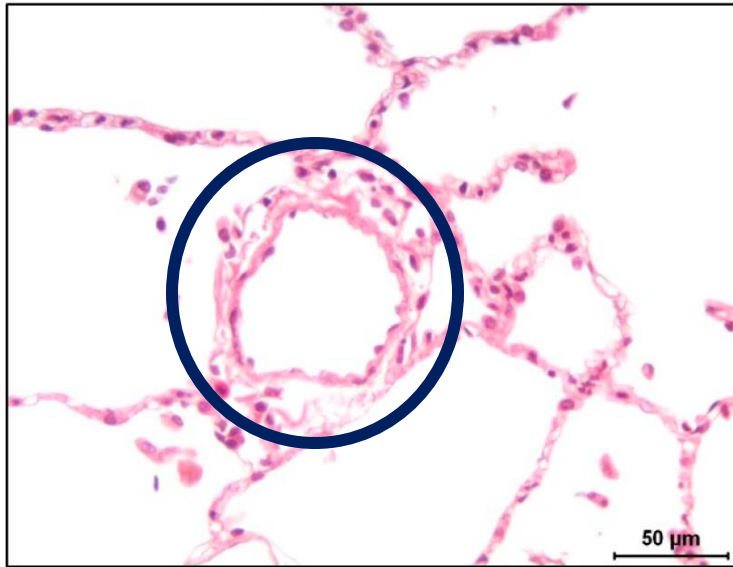
# Early Diagnosis of Lung GVHD is Critical.

## Survival by FEV1 at “Time of Initial Diagnosis” of Lung GVHD



Median FEV1 =  
57% at  
diagnosis of  
Lung GVHD

# The problem is that we start treating here

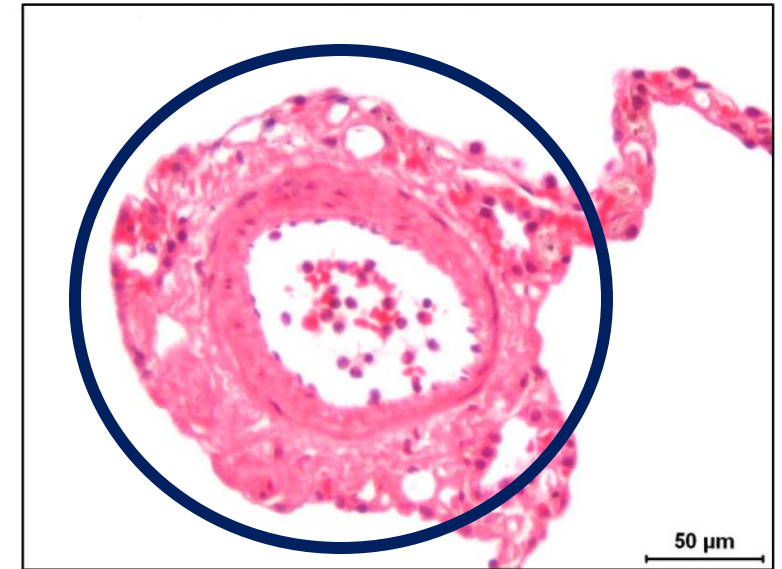
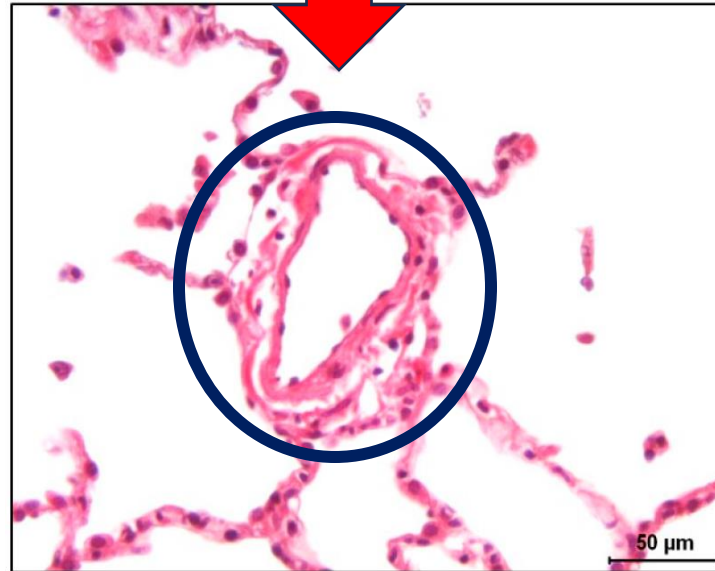
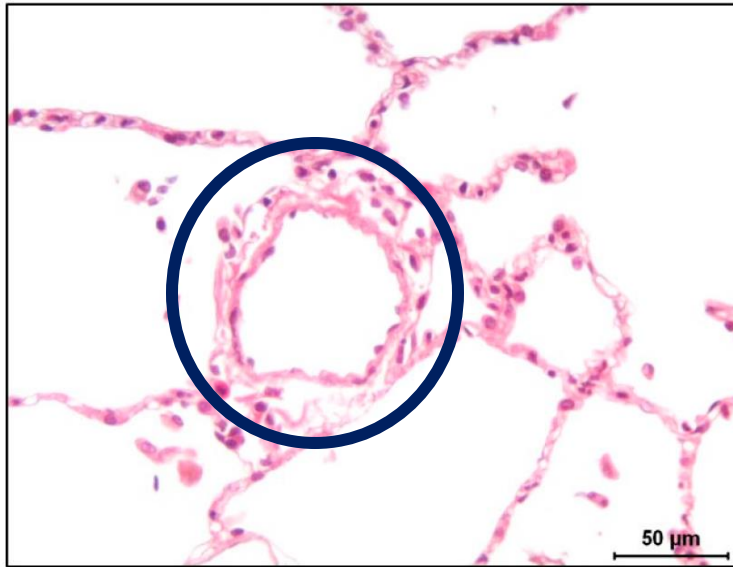


Normal lungs



Lung GVHD  
(Bronchiolitis Obliterans Syndrome)

# We need to be treating here

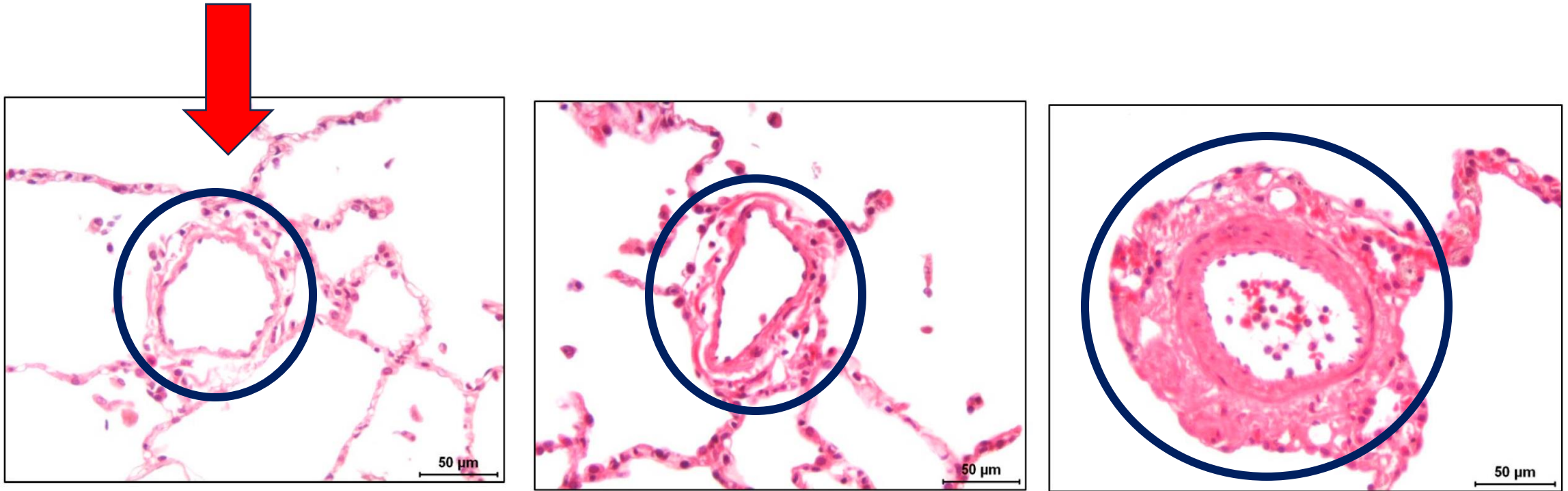


Normal lungs



Lung GVHD

# We need to recognize who's at risk here



Normal lungs



Lung GVHD

(Bronchiolitis Obliterans Syndrome)

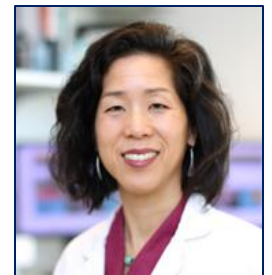
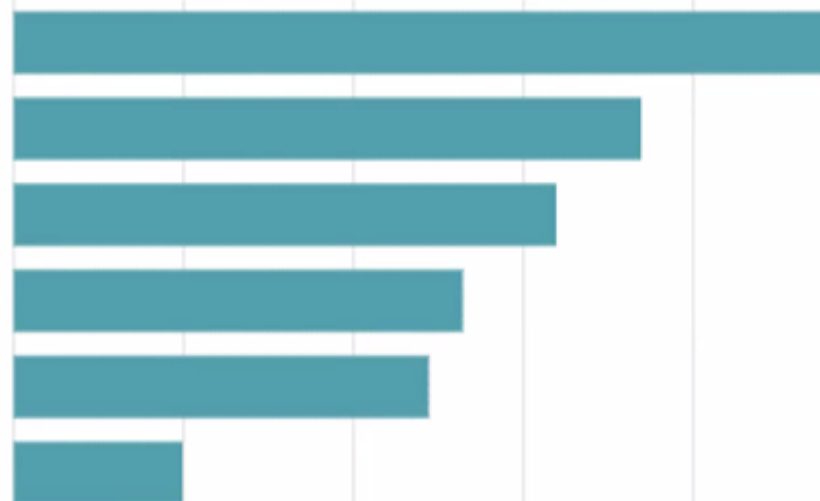
## The patient perspective on early detection

- 54 patient surveys administered via email at 3 sites (FHCC, Stanford, Geneva)
- 30 respondents (55% response rate)

5. What aspects of BOS and lung complications after stem cell transplant should researchers focus on? rank in order of importance (1 to 6; 1 being of highest priority)

[More Details](#)

- 1 Early diagnosis and prevention
- 2 Treatment
- 3 Biological mechanisms
- 4 Patient and clinician education
- 5 Quality of life
- 6 Other - write in next question



Courtesy of Guang-Shing Cheng

# Recommendation for monitoring PFT

“85% of success is just showing up”

- Woody Allen, 1987

Just get PFT's done

# How often should PFT be performed?

## 2020 NIH Consensus Development Project (Kitko TCT 2021)

- Obtain PFT every 3 months for 1<sup>st</sup> year after BMT.
- Once chronic GVHD is diagnosed: Obtain PFT every 3 months.

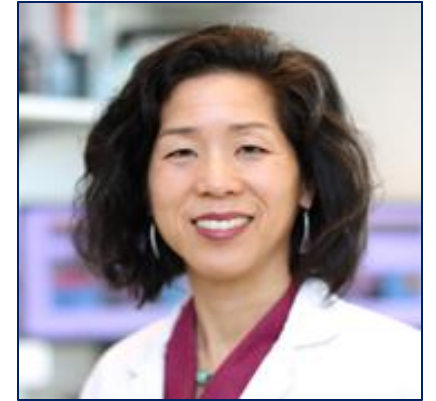


# Issue: Are there alternatives to PFT's?



# PFT testing in your hands

- NIH funded study. Guang-Shing Cheng MD (Seattle)
- Patients perform PFT's weekly, at home.
- Wireless Bluetooth-enabled device.
- Readings sync with patient's smart phone. Patient's can see their FEV1.
- Readings transmitted electronically to MD
- Large, four center study now in progress.

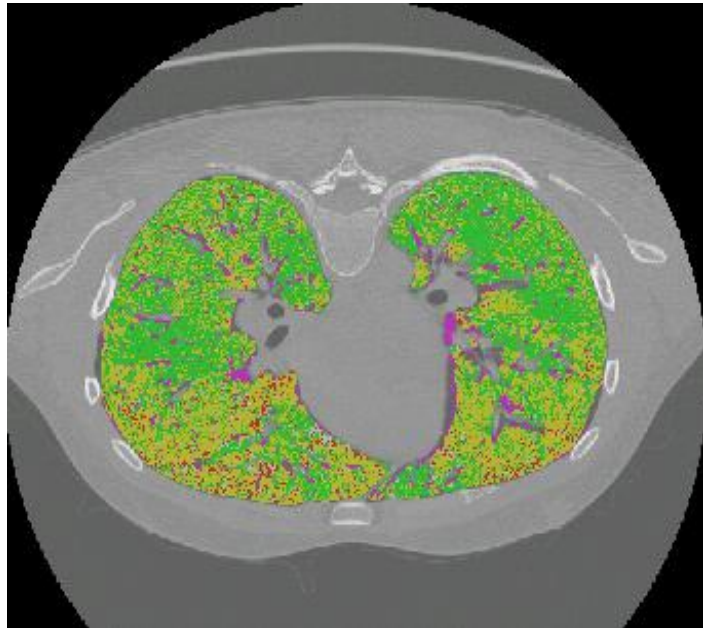


# New CT scan technology: Called PRM

## Color codes the lungs to see areas of lung damage

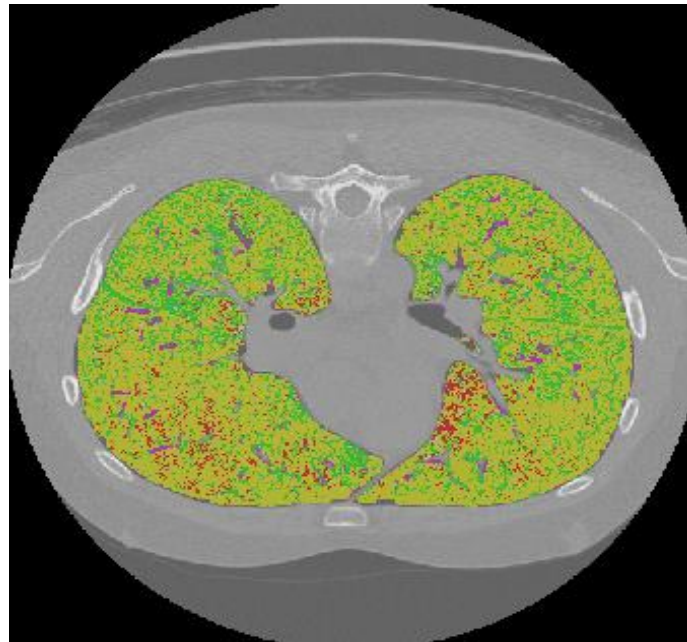
### 1 year post-BMT

Mild lung symptoms.  
PFT and CT both normal



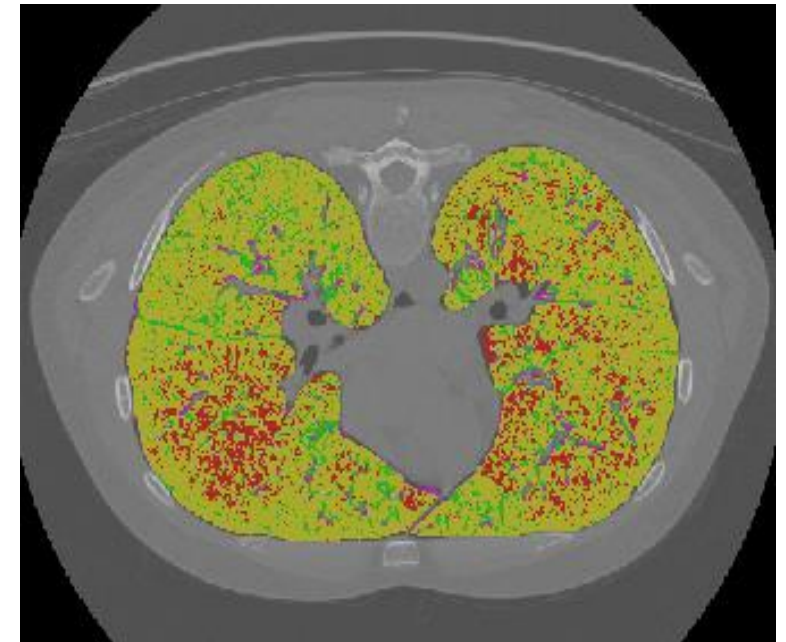
### 2 years post-BMT

Lung GVH is diagnosed



### 5 years post-BMT

Severe symptoms



# Therapy for Lung GVHD

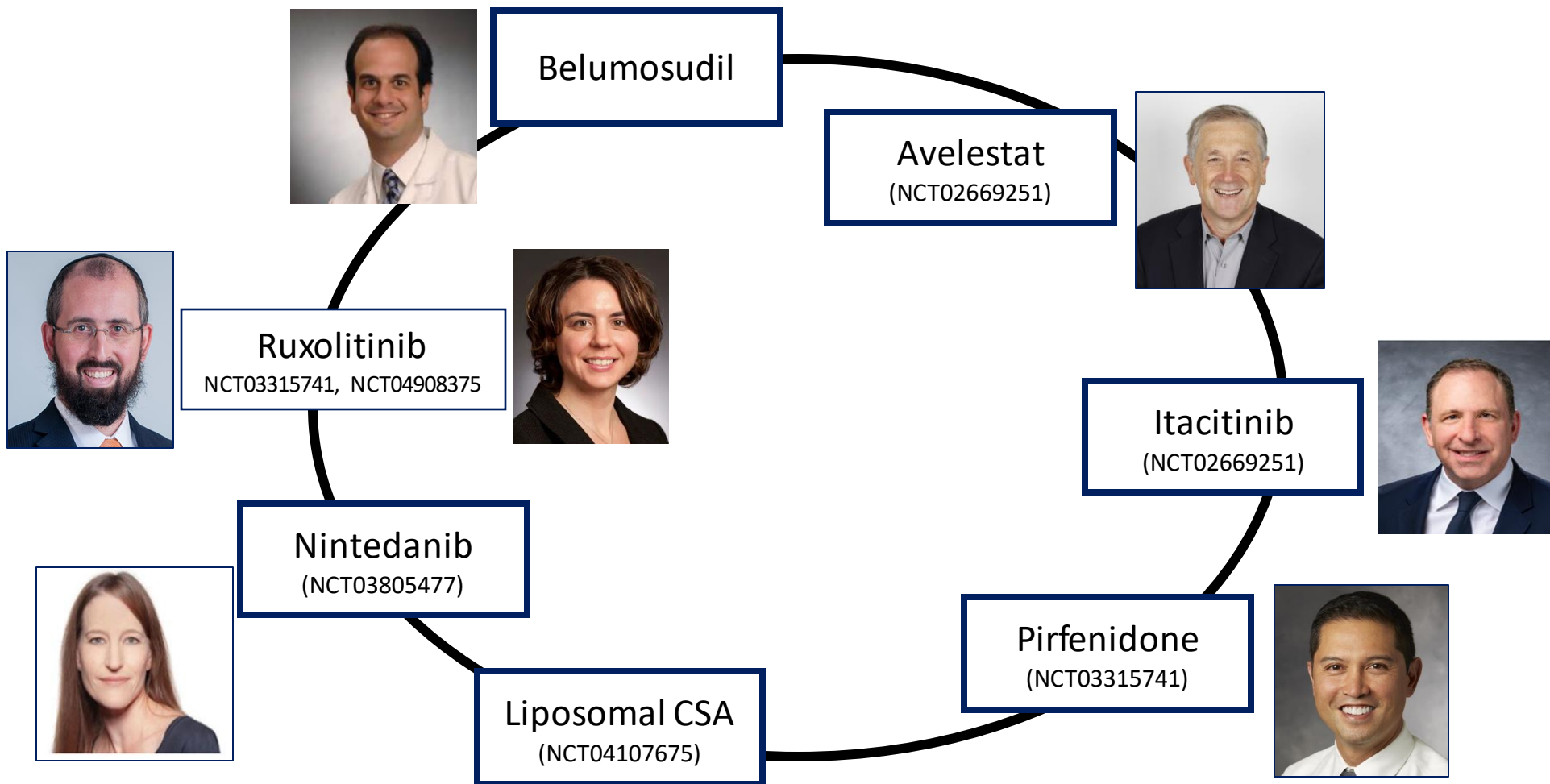
- Few Randomized Clinical Trials
- Two trials that have impacted care:
  - a. Inhaled Steroids (Bergeron A, Am J Respir Crit Care Med. 2015)
  - b. FAM Therapy, n=36 patients (Williams KM, BBMT 2016)

F = Inhaled Fluticasone (inhaled steroid)

A = Azithromycin (oral antibiotic and anti-inflammatory agent)

M = Montelukast (Singular) (oral anti-inflammatory agent)

# Trials for Lung GVHD (BOS) on ClinicalTrials.gov



# Therapy: The power of exercise

PFT report: 50-year-old male with chronic GVHD

		Baseline			Ch
LUNG MECHANICS		Actual	Pred	%Pred	Ac
FVC	liters	3.54	4.47	79%	
FEV1	liters	1.71	3.27	52%	
FEV1/FVC	%	48%	73%	66%	
FEV6	liters	3.16	4.43	71%	
FET	sec	11.91			
FEFMAX	l/sec	3.90	8.72	45%	
FEF25-75	l/sec	0.69	3.28	21%	
FIVC	liters	2.85	4.47	64%	
FIFMAX	l/sec	4.91	8.72	56%	
FIF50	l/sec	4.90	5.19	94%	
FEF50/FIF50	%	17%	100%	17%	
MVV					
LUNG VOLUMES		Actual	Pred	%Pred	Ac
VC	liters	3.54	4.47	79%	
IC	liters	2.49	2.75	91%	
ERV	liters	1.05	1.73	61%	
Sgaw					
DIFFUSION		Actual	Pred	%Pred	Ac
DLCO	ml/min/mmHg	22.20	28.98	77%	
IVC	liters	3.41	3.54	96%	
VA	liters	4.69	6.57	71%	
DLCO/VA	ml/m/Hg/l	4.73	4.41	107%	
Hgb					
DLCOcorrH					

**FEV1 = 52%**  
**DLCO 107%**

**Lung function:**

**Pre-bike riding stage:**

FEV1 = 58%, DLCO = 77%

**After years of bike riding**

FEV1 = 52%, DLCO = 107%

**DLCO measures your ability to transport air into the blood stream.**

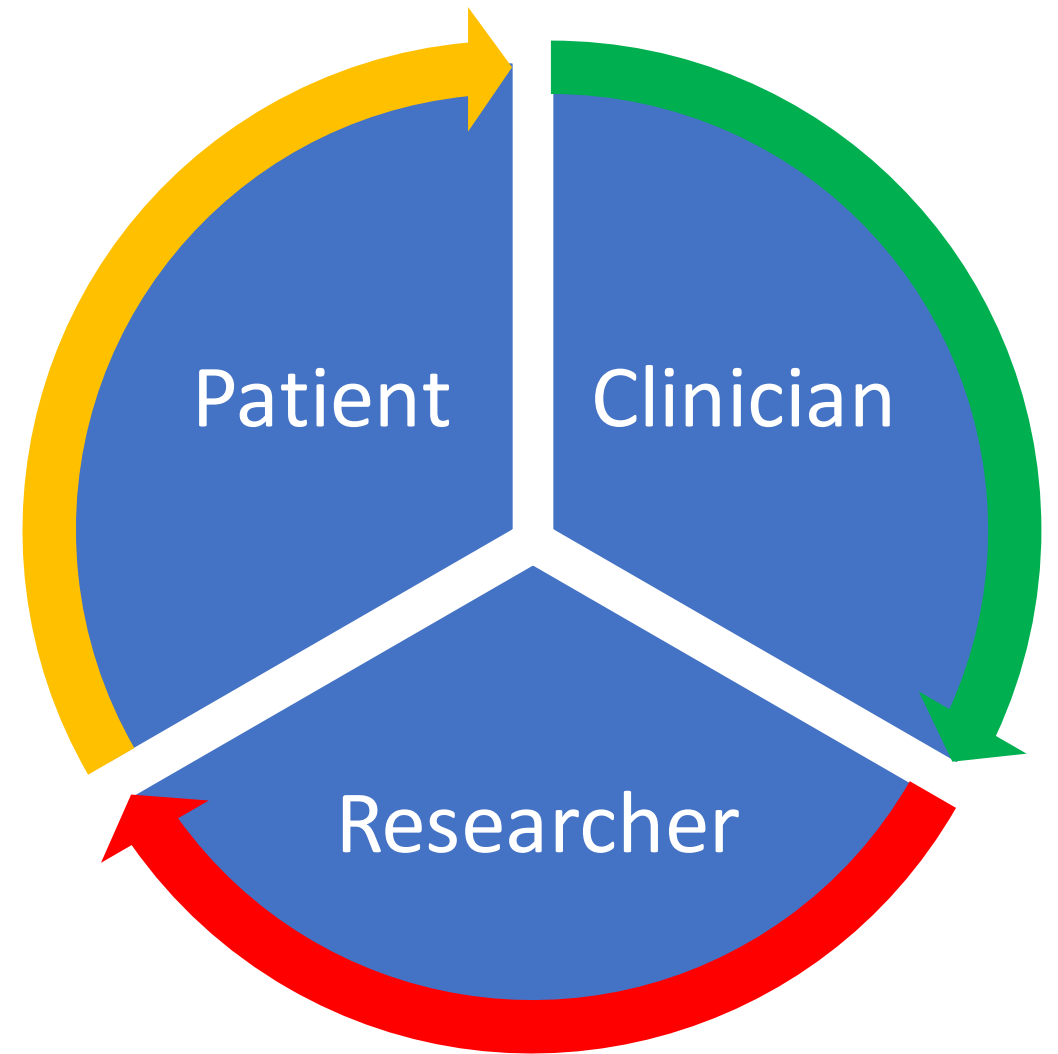


What is the bravest  
thing you've ever said?"  
asked the boy.

"Help," said the horse

*Excerpt from "The Boy, the Mole, the Fox and the  
Horse." - C.Mackesy*

## Circle of Hope



# Thank you everyone.

- To BMT InfoNet.
- To the patients we serve.
- To the medical teams we work with.
- To all of you.

*“Happy are those who dream dreams, and have paid the price to make them come true.” - L.J. Suenens*





# Questions?



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# Let Us Know How We Can Help You

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