



TEST PREP:
A REVIEW OF
THE TESTS
PROVIDERS
PERFORM FOR
MULTIPLE
MYELOMA

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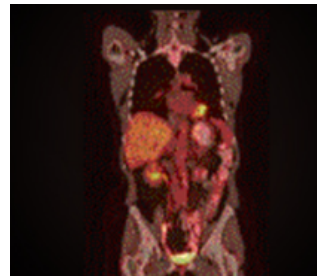
TESTS



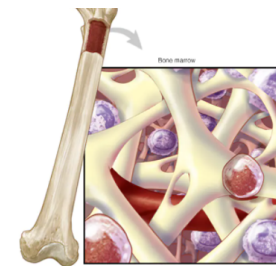
Blood



Urine



Imaging



Bone Marrow

BLOOD

CBC w/differential

CBC w/ANC

BMP

Liver Studies

BMP + Liver = CMP

SPEP

SFLC

Beta 2Albumin/Lactate Dehydrogenase



BLOOD

Diagnosis and Monitoring

Prognosis

Disease Specific Markers

Diagnosis

- CBC
 - Hemoglobin lvls are part of CRAB criteria.
 - ANC, PLT and H/H are monitored to determine impact of disease and negative SE of TX.
- BMP
 - Creatinine and calcium lvls are part of CRAB criteria.
 - Creatinine is a dosing factor for many medications.
- SFLC
 - The number and ratio of abnormal free light chains are part of the MDE.

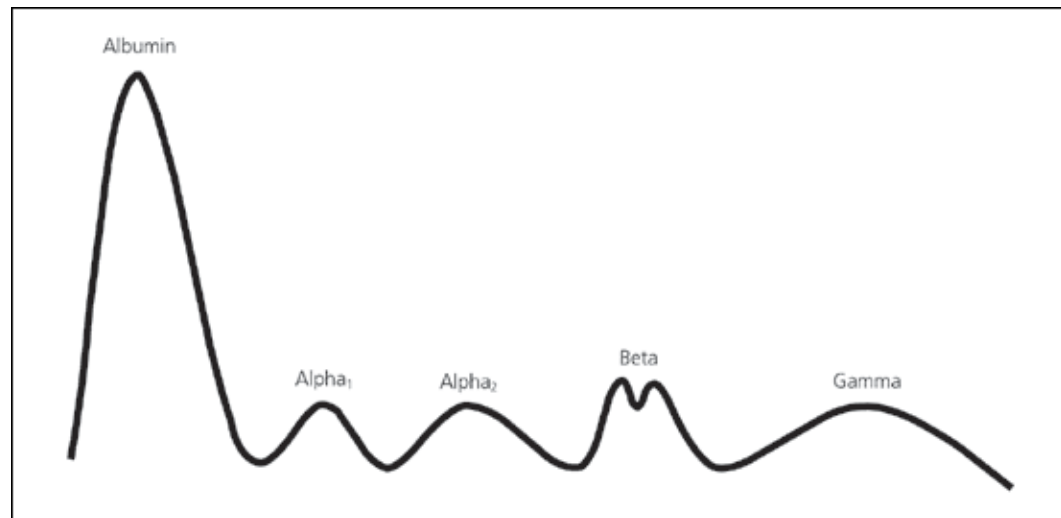
Prognosis

- Beta 2 Microglobulin
 - Serum marker of tumor burden (self vs. non-self)
- Albumin
 - A normal protein in blood
 - Presence of myeloma increases the level of IL-6 in blood.
 - IL-6 blocks the production of albumin
- Lactate dehydrogenase
 - An enzyme *inside* a cell that helps convert sugar into energy.
 - With cell injury or to destruction LDH is leaked into the fluid *outside* the cell.

Disease Specific Markers (Output of Plasma Cells – Not the Plasma Cells Themselves)

- SPEP
 - Electrophoresis divides proteins based on physical properties.
 - An *abnormal* protein will have its own consistent physical properties and form its own spike
 - Estimates the amount of the abnormal protein (M-spike)
- Immunofixation
 - Determines the particular type of abnormal immunoglobulin is in excess
- SFLC
 - Proteins produced by plasma cells (K/L) which bind to heavy chains.

NORMAL ELECTROPHORESIS



URINE

Urine Protein Electrophoresis
Bence Jones



Urine Protein Electrophoresis (UPEP) – 24hr Urine

- Determines the amount of monoclonal protein produced in the marrow, then excreted into the blood and excreted through the kidneys into urine.

Urine Immunofixation (UIFE) – 24hr Urine

- Determines the type of protein that is of monoclonal protein produced in the marrow, then excreted into the blood and excreted through the kidneys into urine

Bence Jones Proteins

- A type of monoclonal protein found in urine that is produced by abnormal plasma cells in marrow.



Henry Bence Jones

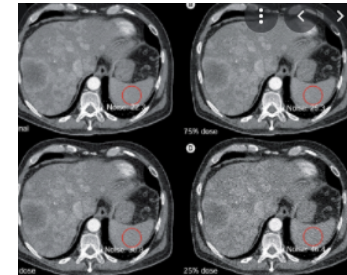
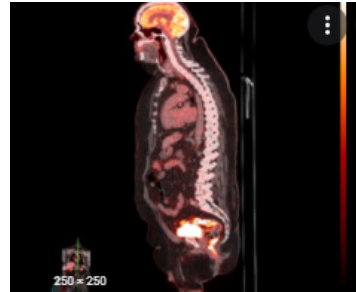
IMAGING

XR/OS

MRI

PET CT

(HS)WBLDCT





X-Ray

The osseous survey was a whole-body x-ray that was the gold standard for decades to assess multiple myeloma's impact on the skeleton.

Pros

- Inexpensive and widely available.
- Quick to schedule
- Quick to get results
- Excellent at detecting gross lesions or fractures
- Low radiation

Cons

- Misses approximately 30% of subtle lytic lesions
- Lytic lesions are only detectable if >30% of trabecular bone is destroyed.

Conclusion:

Single x-rays are good for quickly trying to detect an acute fracture or more-than-subtle lytic lesion. The osseous survey is not an ideal imaging system for disease diagnosis.



MRI (non-contrast)

Magnetic resonance imaging (MRI) creates very detailed images of the human body.

Pros

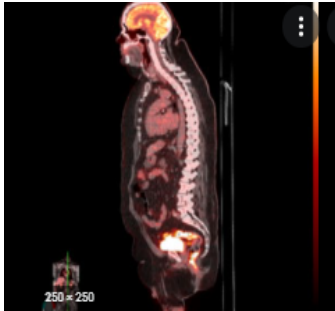
- No radiation
- Ideal for initial evaluation of single plasmacytoma in bone (osseous) of the spine or pelvis as well as spinal cord and nerve roots (compressions).
- Good at discerning between smoldering and true multiple myeloma.
- A good scanning option if CT is not available.
- Very sensitive at detecting marrow infiltration, lesions and differentiate between normal and abnormal marrow.

Cons

- Cannot identify level of disease activity.
- Longs scanning time and uncomfortable for certain patients.

Conclusion:

Excellent for detecting very subtle lytic lesions (good for diagnosis) and detecting abnormalities in spine and pelvis.



PET/CT

PET/MRI

A combined test using a radiotracer (radioactive sugar – see SUV levels) to detect level of disease activity with the fine depiction of bony structures and lesions.

Pros

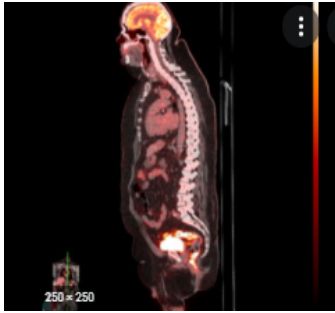
- Highly sensitive for diagnosis/staging/response/relapse.
- Gets both structural and metabolic information.
- Highly sensitive and can detect isolated lesions.

Cons

- Radiation
- Use of growth factors can impact results.
- Expensive – Can be difficult to get cleared with certain insurance plans.

Conclusion:

A very sensitive test that can be used in a host of situations.



(HS)WBLDCT

The newest method of imaging for MM. Used to identify bone damaging (osteolytic) lesions in the entire skeleton.

Pros

- Highly sensitive for diagnosis/staging/response/relapse.
- Does not require contrast.
- Low radiation
- Highly available (in theory)
- Fast, more comfortable than MRI

Cons

- Doesn't give levels of metabolic activity.
- Not as sensitive as MRI.
- Requires specialized training for radiology staff.

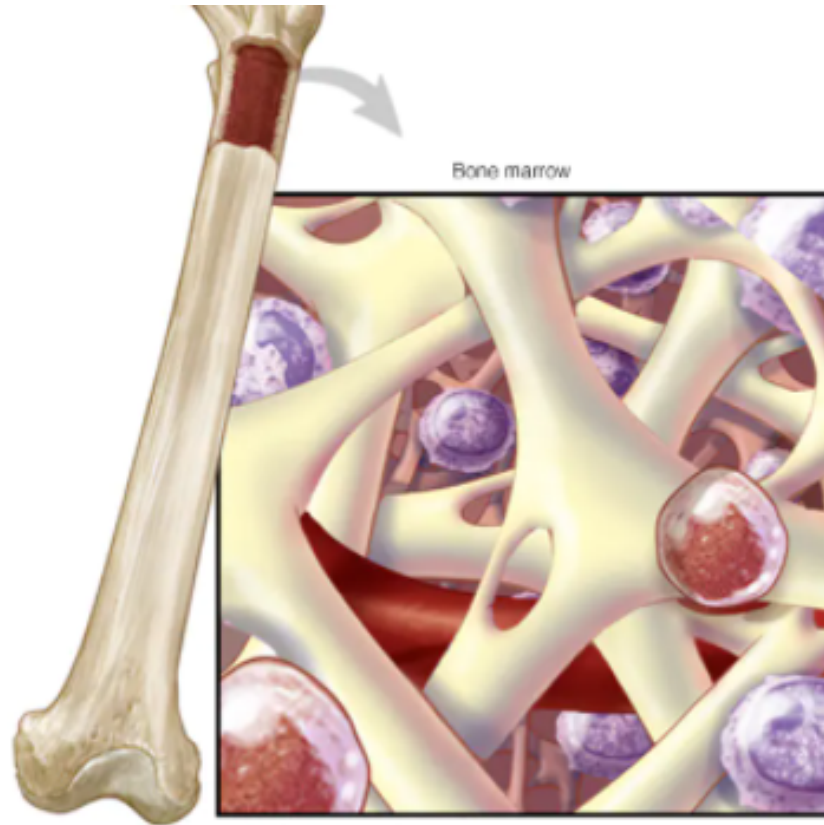
Conclusion:

A very sensitive test that can be used in a host of situations. Low cost and highly sensitive.

MARROW

Aspirate/Marrow

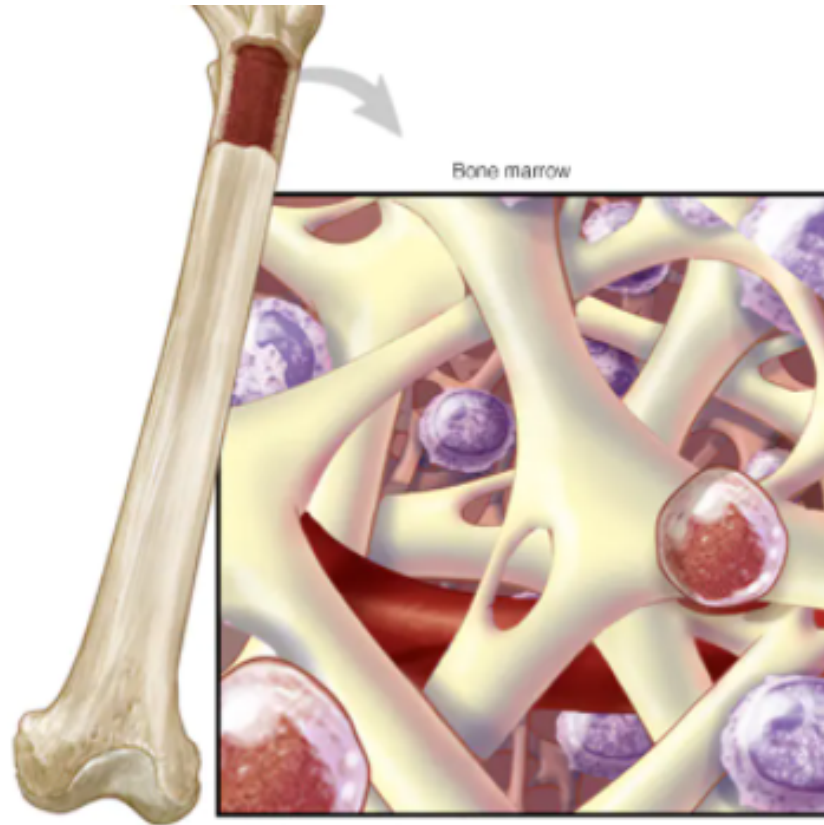
Hematopathology
Flow cytometry
Cytogenetics
MRD by NGS



Some quick notes about sedation:

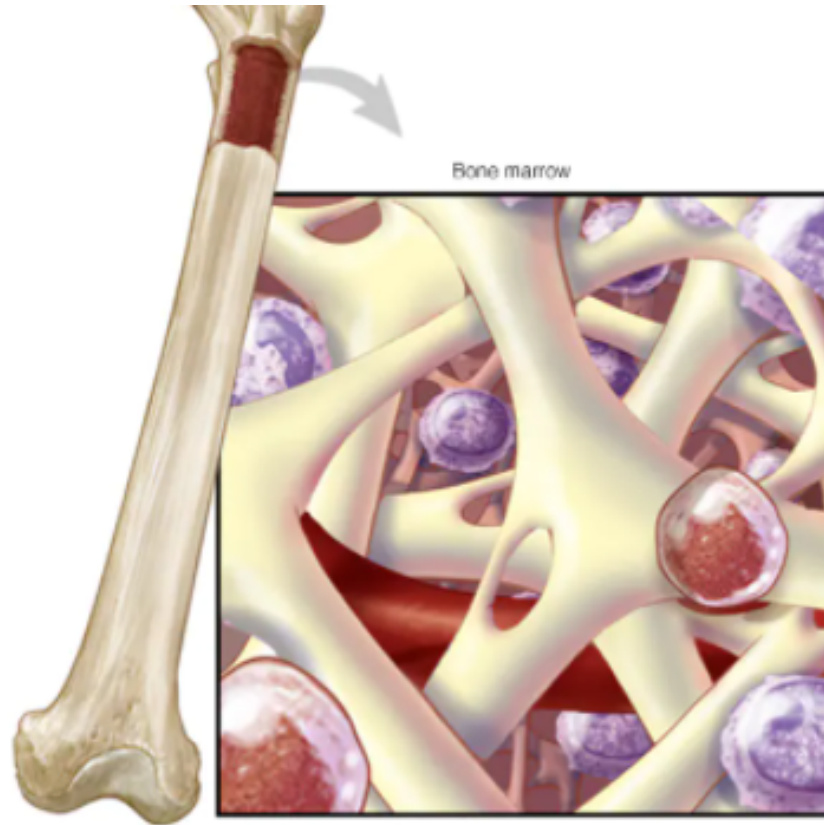
1. Everyone gets lidocaine or a similar local anesthetic. If you only receive lidocaine this is called **NO SEDATION**.
2. If you receive an opioid based pain reliever (i.e. oxycodone) or an anti-anxiety medication (i.e. Ativan) at the procedure suite before the procedure this is **MINIMAL SEDATION**. You cannot receive both medications together any longer.
3. **CONSCIOUS SEDATION** is where you receive IV fentanyl (a synthetic opioid) and an IV anti-anxiety (i.e. midazolam). The goal is not to put the patient to sleep but just to make it hard to remember the procedure. Like a COLO.
4. **GENERAL ANESTHESIA** is like surgery. The patient is unconscious during the procedure.

NOTE: The more anesthesia required the longer it takes to schedule.



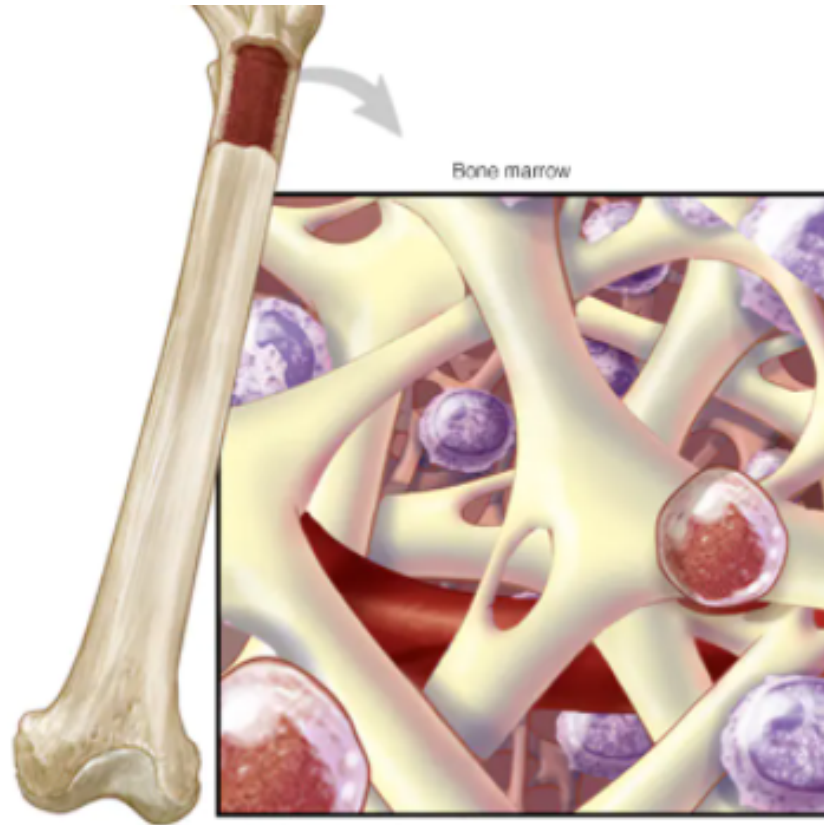
Aspirate: The liquid portion of the procedure. Fluid that surrounds the trabeculae is drawn out. This takes cells and pieces of trabeculae with it. Drawn from inside the bone.

Marrow: A core sample that begins on the surface of the bone and extends into the trabecular area.

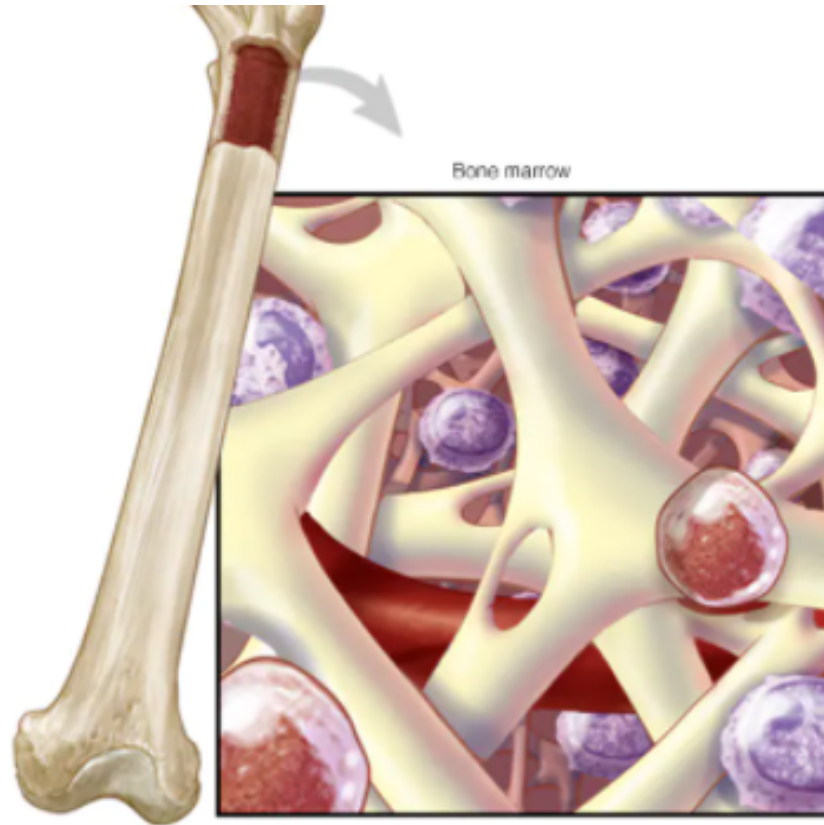


Hematopathology:

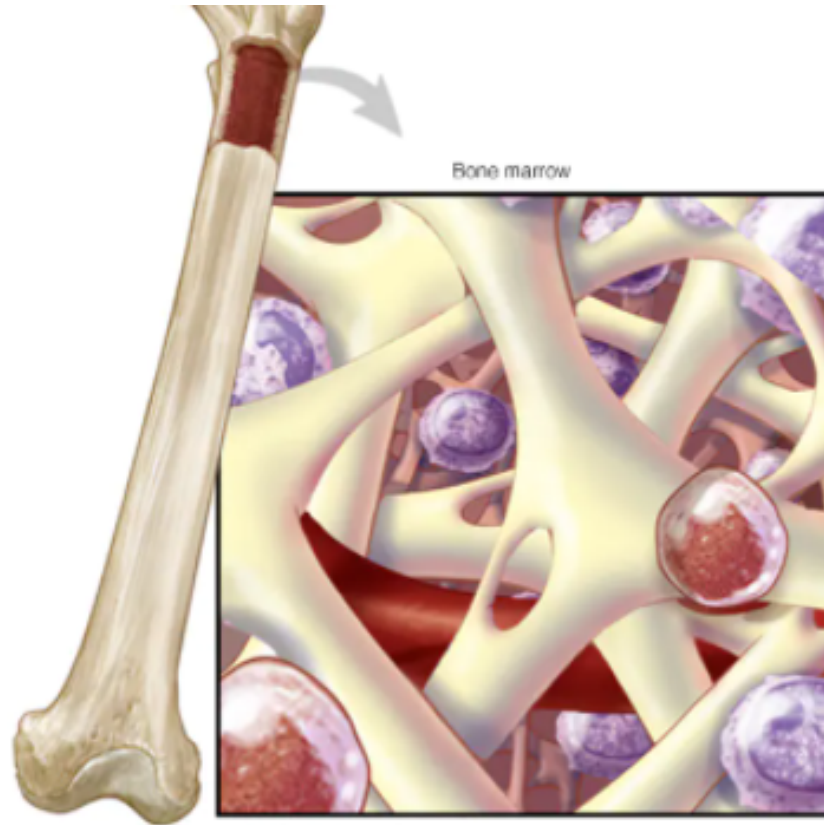
A microscopic review of the material from a bone marrow aspirate/biopsy. A laboratory technician looks at a slide of marrow material and counts the number of abnormal plasma cells they see. It is given in a percentage (For example: 30% abnormal plasma cells).



Flow Cytometry: Collected cells receive a bath of light sensitive dye and are passed one at a time through a beam of light. Based on how the stained cells respond to the light help identify the characteristics of the cell.



Cytogenetics: A test to determine the unique genetic makeup of a patient's multiple myeloma. It identifies high-risk cytogenetics as well as genetic abnormalities that will help guide treatment and inform prognosis.

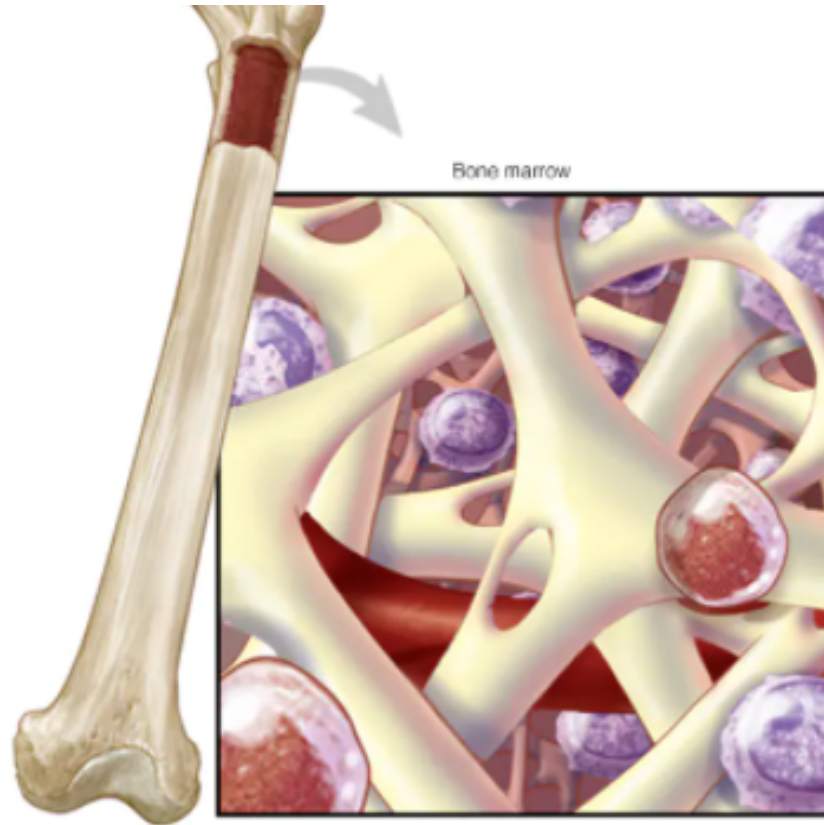


MRD by NGS:

Minimal Residual Disease

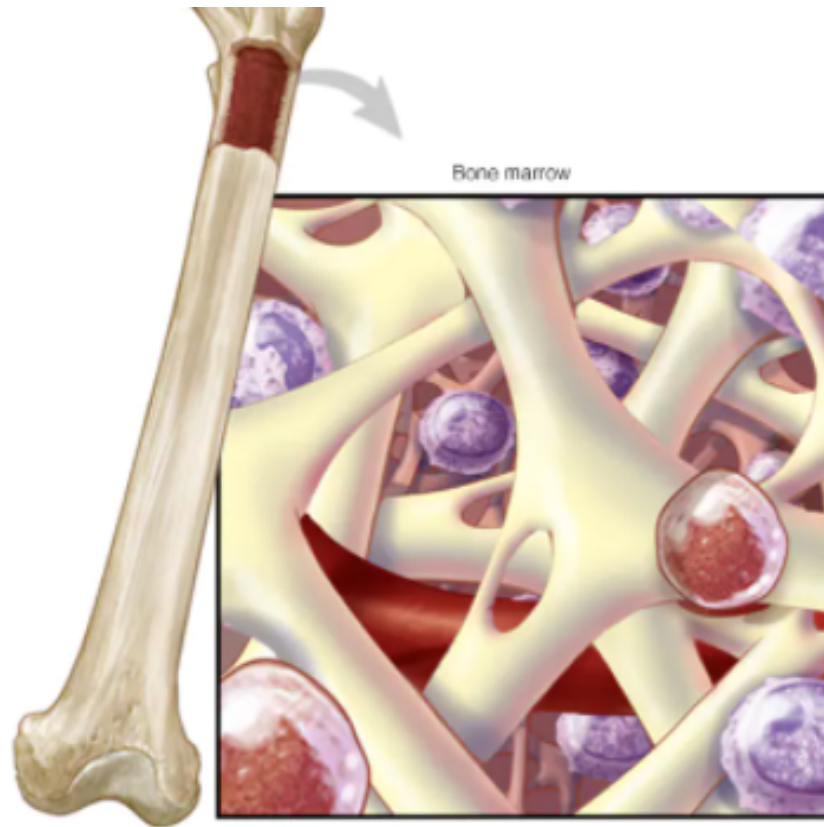
by

Next Generation Sequencing



Minimal Residual Disease: Is a measurement of the remaining detectable disease *after* treatment.

Next Generation Sequencing: A fast, accurate method of determining the level of minimal residual disease using the unique DNA sequence of a patient's cancer.

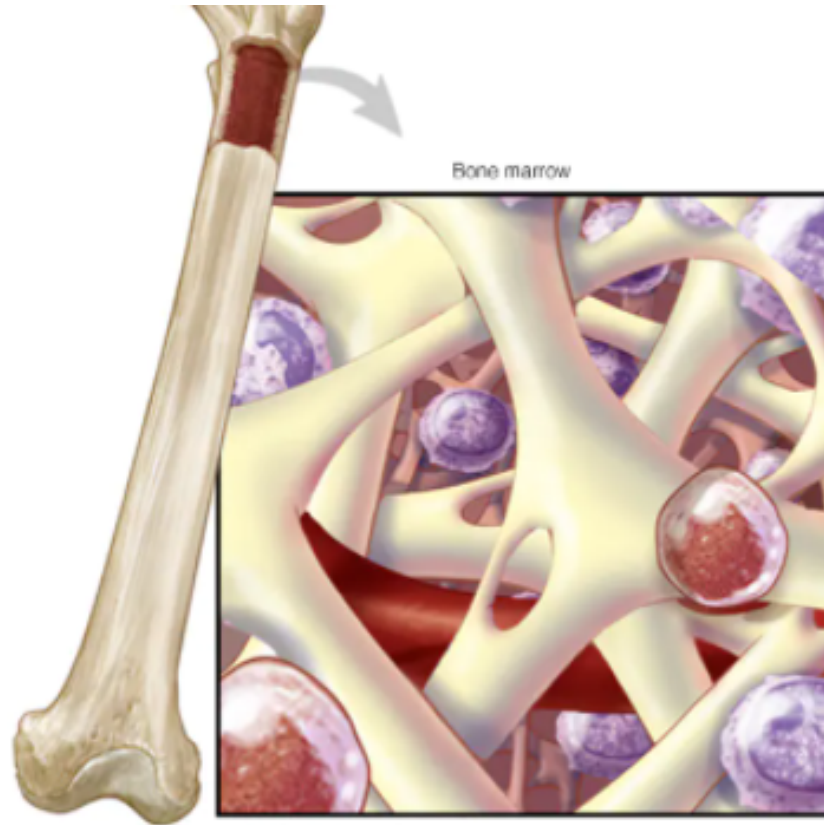


Each B-cell has a unique structure that makes it different from other B-cells.

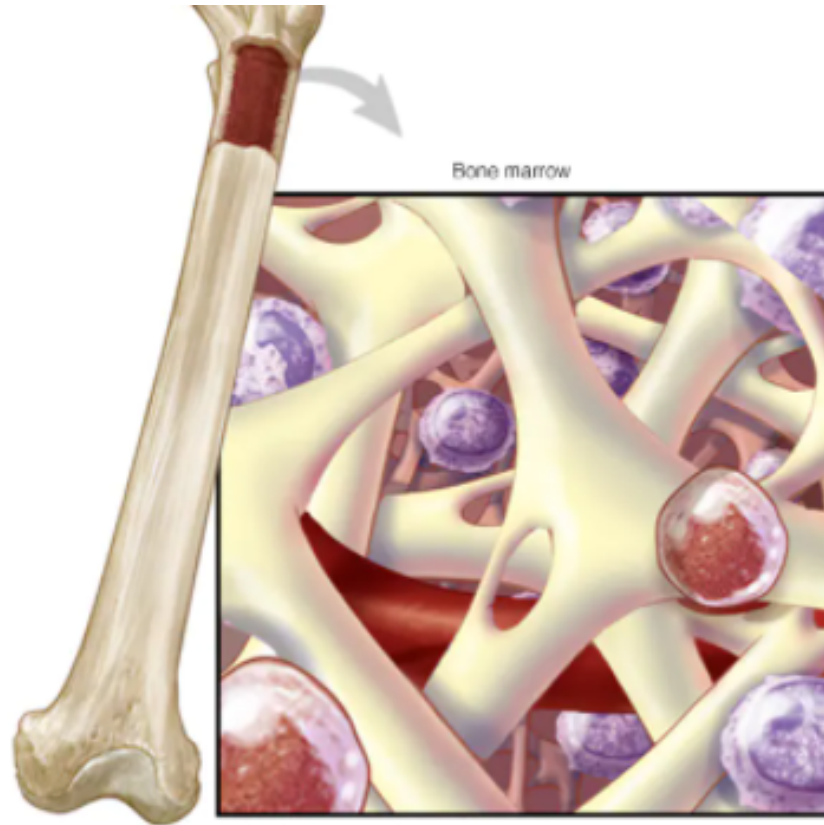
CDR3 is the region in DNA where each of these unique arrangements occur.

With MM the abnormal B-cells have their own unique CDR3 area rearrangement.

NGS uses this unique CDR3 sequence to identify the level of a patient's response to treatment.



Simply put, the lower the amount of this unique arrangement we find, the deeper the response to treatment.





← CDR3 region with normal arrangement



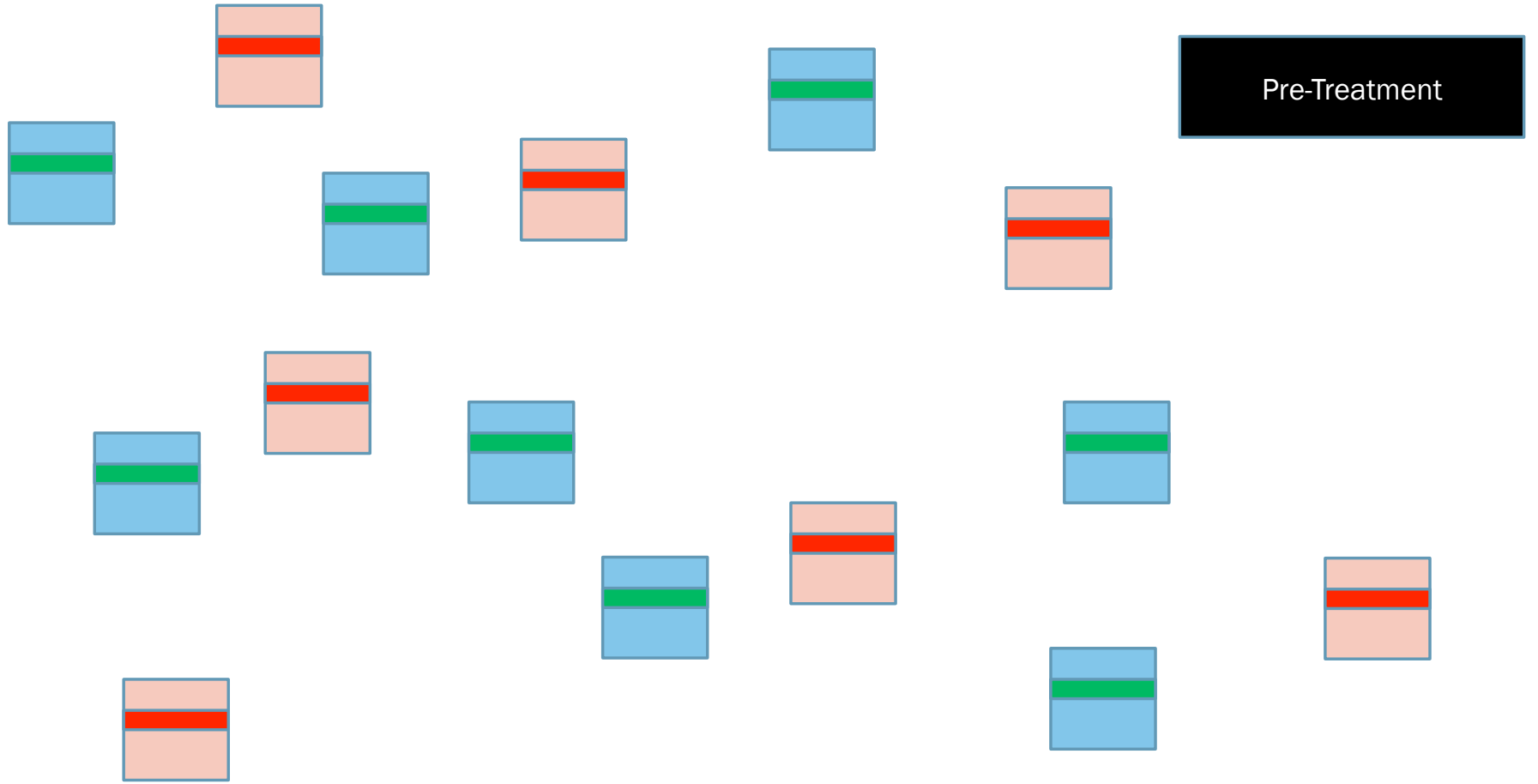
Normal plasma cell

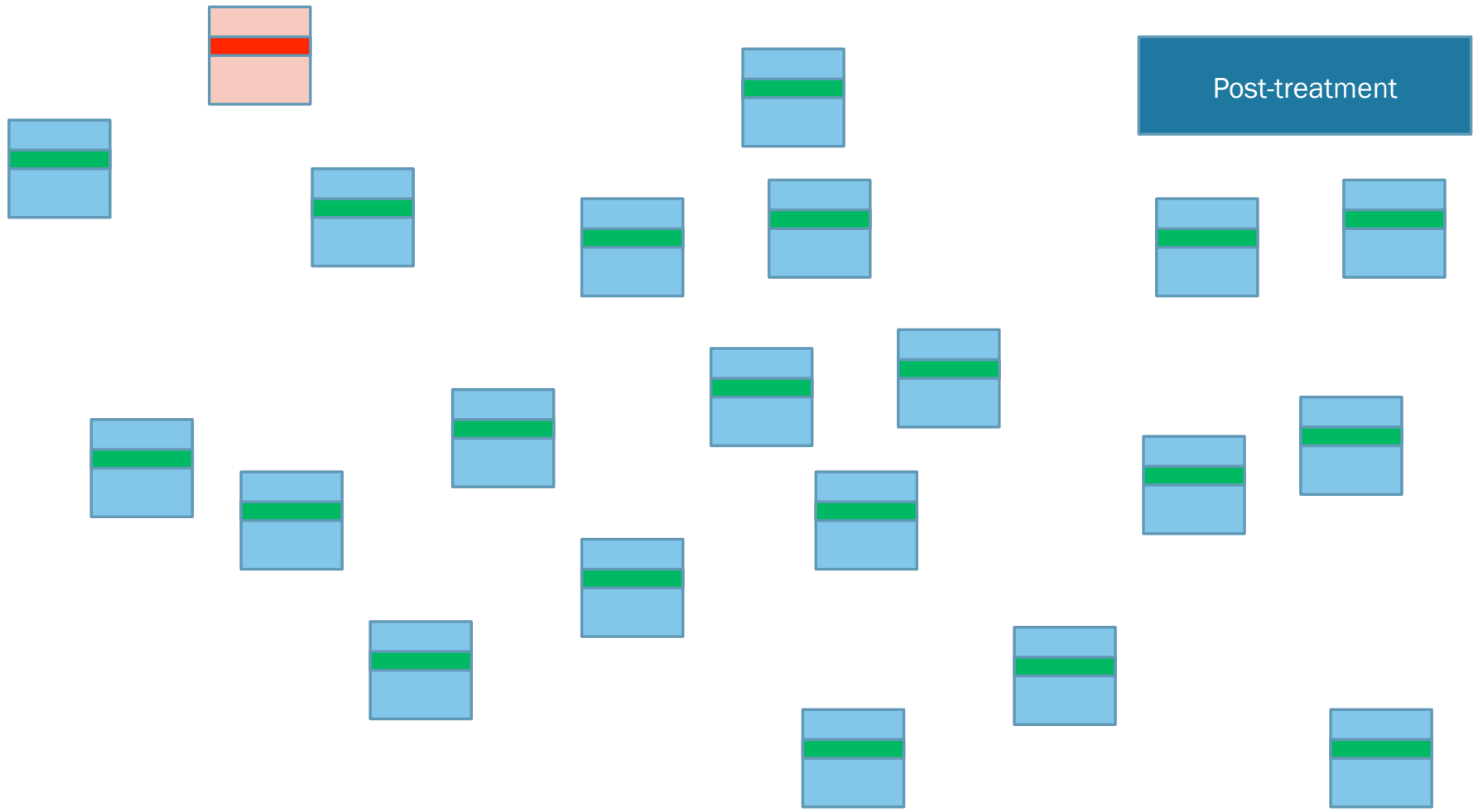


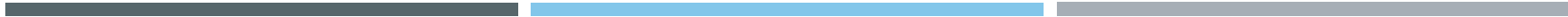
← CDR3 region with abnormal arrangement



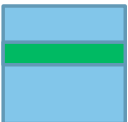
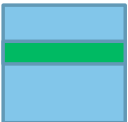
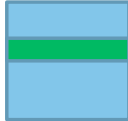
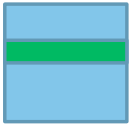
Abnormal plasma cell

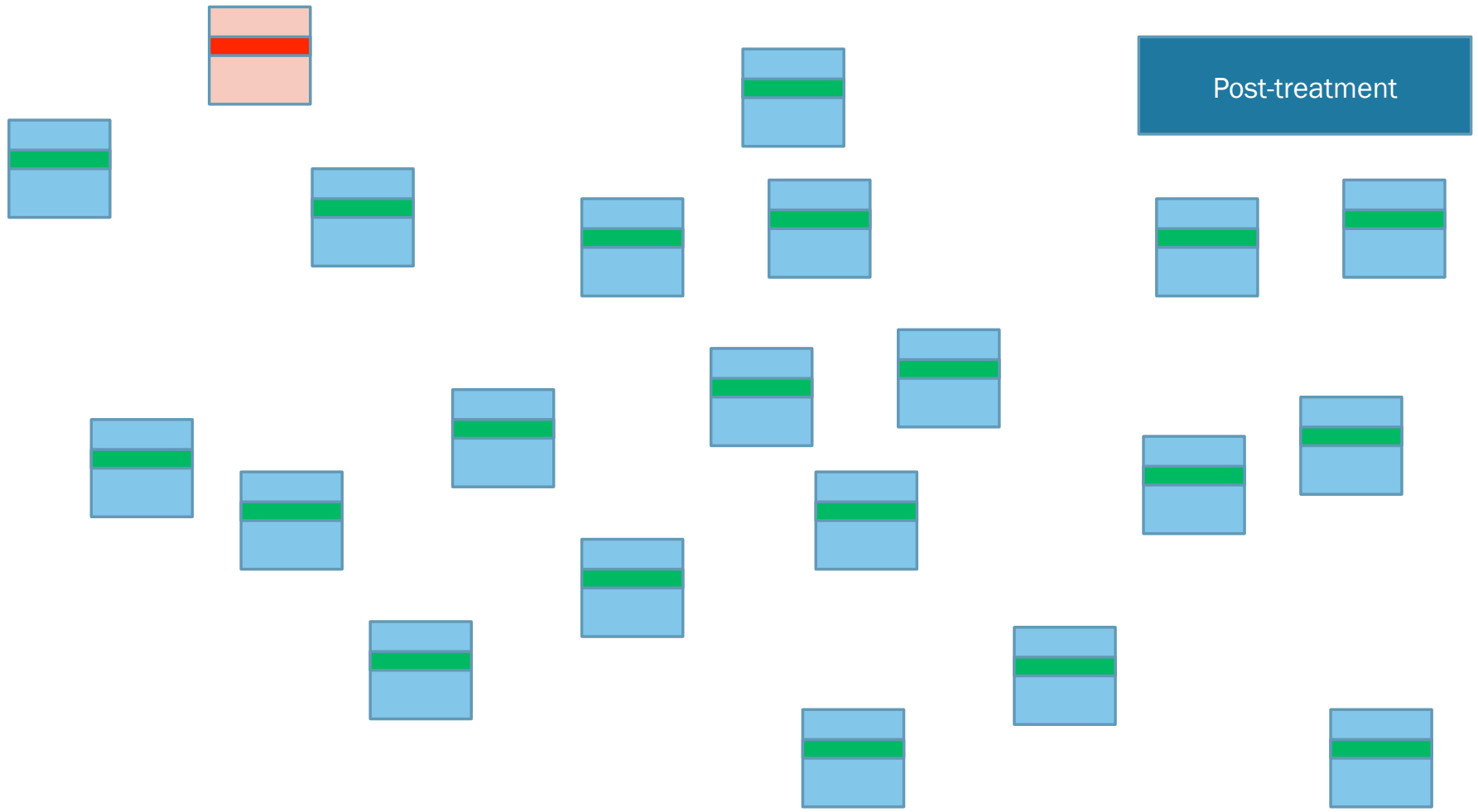






Post-treatment



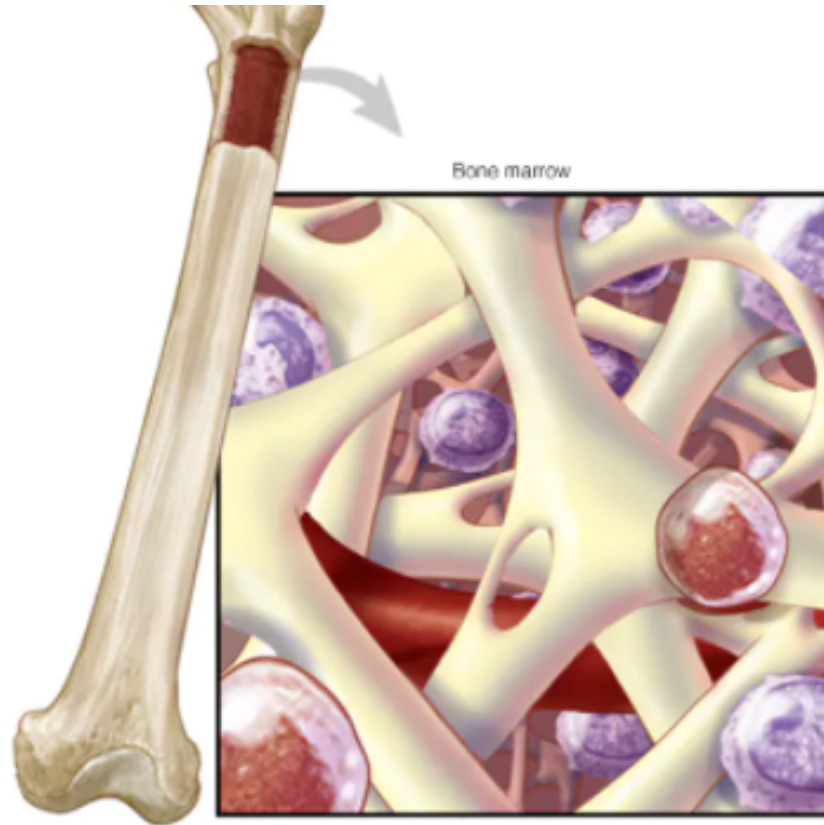


The number of times we find



Tells us how much disease is left.

What do we do with this information?



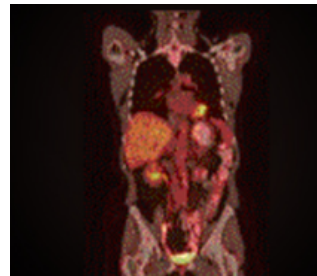
DIAGNOSIS, TREATMENT, DETERMINATION AND DURABILITY OF RESPONSE ALL DEPEND ON THESE TESTS



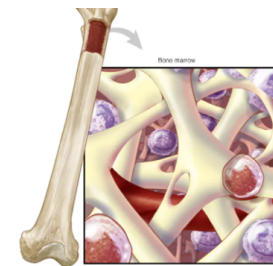
Blood



Urine



Imaging



Bone Marrow

QUESTIONS?