QUALITY PROCESSES

WORKFLOW

- FOLLOW A SPECIMEN FROM PHYSICIAN ORDER TO REPORTED RESULT
- FLOW CHART
- DOCUMENTATION

PROCESSES

- PRE-ANALYTICAL
- ANALYTICAL
- POST-ANALYTICAL
- EQUIPMENT & REAGENTS
- QUALITY ASSURANCE

PRE-ANALYTICAL

- SPECIMEN COLLECTION
- SPECIMEN TRANSPORT
  - INTERNAL AND EXTERNAL
- RECIEPT OF SPECIMEN IN LAB
  - LABELLING
  - ACCESSIONING
- REQUISITIONS

ANALYTICAL

- METHODS

  CURRENT
  - BASED ON PUBLISHED PRACTICE GUIDELINES OR IN-HOUSE PROCEDURES VALIDATED BY THE LABORATORY
  - APPROVED BY LABORATORY DIRECTOR/DESIGNEE
- DOCUMENTATION OF PROCEDURES
- AVAILABLE AT WORKSTATION FOR END USER
- ANNUAL REVIEW

POST-ANALYTICAL

- REPORTING
- TAT, STAT
- RECORD RETENTION

EQUIPMENT & REAGENTS

- EQUIPMENT
  - NEW EQUIPMENT
  - EXISTING EQUIPMENT

- NEW EQUIPMENT
  - MARKET EVALUATION
  - MANUFACTURERS PERFORMANCE CLAIMS MUST BE VALIDATED PRIOR TO USE

EXISTING EQUIPMENT

- SERVICE RECORDS
  - AUTOSTAINERS, MICROSCOPES
  - ROUTINE PM, SERVICE/PROBLEM DOCUMENTATION
- MAINTENANCE RECORDS
  - CLEANING
  - REPLACEMENT OF SCHEDULED PARTS
  - pH STANDARDIZATION
- CALIBRATION AND VERIFICATION
  - PIPETTES, SCALES

- TEMPERATURE DEPENDANT
  - DAILY CHECK OF TEMPERATURE
    or DAY OF USE
  - MONITORING DEVICES WITH ALARMS
  - INTERNAL THERMOMETER (NIST CERTIFIED)
- UP-TO-DATE INSTRUCTIONS
  - ALL RECENTLY APPROVED
  - AVAILABLE AT THE WORK BENCH

EQUIPMENT & REAGENTS

- REAGENTS
  - STORAGE REQUIREMENTS
  - INSPECTION, ACCEPTANCE/REJECTION
    - OLD BATCH, NEW BATCH COMPARISON
  - VERIFY PERFORMANCE PRIOR TO USE
    - pH, RESULT COMPARISON

REAGENTS

- INVENTORY CONTROL
- RECORD KEEPING
  - LOT #, EXPIRY DATE, DATE IN SERVICE, CONDITIONS
- WHMIS
- WATER
  - CRITERIA FOR WATER THE WATER QUALITY USED IN TESTING

QUALITY ASSURANCE

- INTERNAL QUALITY CONTROL
- INTERLABORATORY COMPARISON
- EXTERNAL QUALITY ASSESSMENT

INTERNAL QUALITY CONTROL

- POLICY & PROTOCOL ESTABLISHED
- ASSESS WITHIN EACH USER-DEFINED RUN
- POSITIVE AND NEGATIVE CONTROLS
- CONTROLS TO BE TREATED IN THE SAME MANNER AS THE PATIENT SAMPLE
- NEW REAGENT LOTS ARE CHECKED PRIOR TO USE AGAINST :PRIOR REAGENT LOT OR REFERENCE MATERIAL

INTERLABORATORY COMPARISON

- An evaluation of performance and/or laboratory competence in the testing of defined samples by two or more laboratories

- Inter/Intra Laboratory comparison
  - Case/Control Review
  - Histo/Cyto Correlation

EXTERNAL QUALITY ASSESMENT

- PROFICIENCY TESTING:
  INTER- LABORATORY
  * If there is no formal EQA program, some mechanism to compare results with other sites

- PEER REVIEW ASSESSMENT

- ENSURING THE QUALITY OF THE LAB'S RESULTS TO DETERMINE ACCURACY AND RELIABILTY OF THE PROCEDURE

VALIDATION PROCESS

DEFINITION

- VALIDATION REFERS TO ESTABLISHING DOCUMENTED EVIDENCE THAT A PROCESS OR SYSTEM, WHEN OPERATED WITHIN ESTABLISHED PARAMETERS, CAN PERFORM EFFECTIVELY AND REPRODUCIBLY TO PRODUCE PREDETERMINED SPECIFICATIONS AND QUALITY ATTRIBUTES

VALIDATE WHAT?

- ANTIBODIES
- DETECTION SYSTEMS
- CHROMOGENS
- PRETREATMENTS
- BUFFERS
- ANCILLARY PRODUCTS

ANTIBODIES

- CLONE
- STORAGE CONDITIONS/TEMPERATURE
- SUPPLIER/MANUFACTURER INFORMATION
- LOT #
- EXPIRY DATE
- ISOTYPE/ CONCENTRATION
- ANTIBODY DILUTION
- INCUBATION TIME/ TEMPERATURE
- PRETREATMENTS
- DETECTION SYSTEM
- CONTROL TISSUE
- SIGNATURES

ANTIBODY TECHNICAL INFORMATION

Antibody: _____ **Clone:**_____

Source: Mouse Monoclonal ( ) Rabbit Polyclonal ( ) Others: _____
Manufacturer: **CAT. No.:** **Supplier:**
Lot: **Expiry Date:**
Isotype: **Total or Ig Concentration:** **Negative Dilution:**
Form: Concentrated Solution ( ) Lyophilized Power ( ) Prediluted Solution ( )
Storage Conditions: Refrigerator, 4-8 ºC ( ) Deep Freezer, - 70 ºC ( )
Optimized Staining Conditions:
Method: ( ) ABC-Elite (Vector Labs. Inc. ( ) UV (Ultra Vision)
( ) USA (Signet Labs. Inc.) ( ) DIF (Direct Immunofluorescence)

Pretreatment Testings:

Pretreatment	Results	Selectio
MAR -Citrate		
MAR – EDTA or TRIS HCL		
Pepsin		
NIL		
Others		

Done By:
Date:
Comments:
Recommended Positive Control:
Initial Date of Use: _____
Retirement Date: _____ **Reason:**

ANTIBODY RECORD

ANTIBODY:_____

DATE REC'D	MANUFACT/ SUPPLIER	LOT #	EXPIRY DATE	ISO-TYPE	CONC	DATE IN SERVICE	DILUTION	PTM	SYSTEM	MLT

DETECTION SYSTEMS

- INSPECTION
- DOCUMENTATION
  - LOT NUMBER, EXPIRY DATE, DATE CHECKED, DATE RECEIVED, DATE OPENED, MLT INITIALS
- ACCEPTANCE/REJECTION
  - OLD BATCH, NEW BATCH COMPARISON

CHROMOGENS

- INSPECTION
- DOCUMENTATION
  - LOT NUMBER, EXPIRY DATE, DATE CHECKED, DATE RECEIVED, DATE OPENED, MLT INITIALS
- ACCEPTANCE/REJECTION
  - OLD BATCH, NEW BATCH COMPARISON

PRETREATMENTS

COMMERCIALLY PREPARED

- INSPECTION
- DOCUMENTATION
  - LOT NUMBER, EXPIRY DATE, DATE CHECKED, DATE RECEIVED, DATE OPENED, MLT INITIALS
- ACCEPTANCE/REJECTION
  - OLD BATCH, NEW BATCH COMPARISON

PREPARED IN-HOUSE

- DOCUMENTATION
  - DATE PREPARED, DATE OPENED,DATE CHECKED, MLT INITIALS
- ACCEPTANCE/REJECTION
  - OLD BATCH, NEW BATCH COMPARISON

BUFFERS

COMMERCIALLY PREPARED

- INSPECTION
- DOCUMENTATION
  - LOT NUMBER, EXPIRY DATE, DATE CHECKED, DATE RECEIVED, DATE OPENED, MLT INITIALS
- ACCEPTANCE/REJECTION
  - OLD BATCH, NEW BATCH COMPARISON

PREPARED IN-HOUSE

- DOCUMENTATION
  - DATE PREPARED, DATE OPENED,DATE CHECKED, MLT INITIALS
- ACCEPTANCE/REJECTION
  - OLD BATCH, NEW BATCH COMPARISON

ANCILLARY PRODUCTS

- HEAMATOXYLIN
- DILUTING BUFFERS

ER and PgR evaluation

Clinical validation:

- Test identifies subets of patients with significantly different risks of recurrence/survival

Technical validation:

- Test is sensitive, specific, reproducible and interpreted in a uniform manner from lab to lab

ER and PgR evaluation

Technical validation:

- Sensitive
- Specific
- Reproducible
- Interpreted in uniform manner from lab to lab

ER evaluation

Technical validation:

- Sensitive – *several abs*
- Specific – *several abs*
- Reproducible – *different IHC methods*
- Interpreted in uniform manner from lab to lab – *arbitrary cut-offs and methods of scoring*

ER and PgR evaluation

IHC:

- Signals difficult to quantify
- Results affected by:
  - tissue handling/fixation/processing
  - specificity/sensitivity of primary ab
  - detection systems
  - antigen retrieval
  - methods of scoring

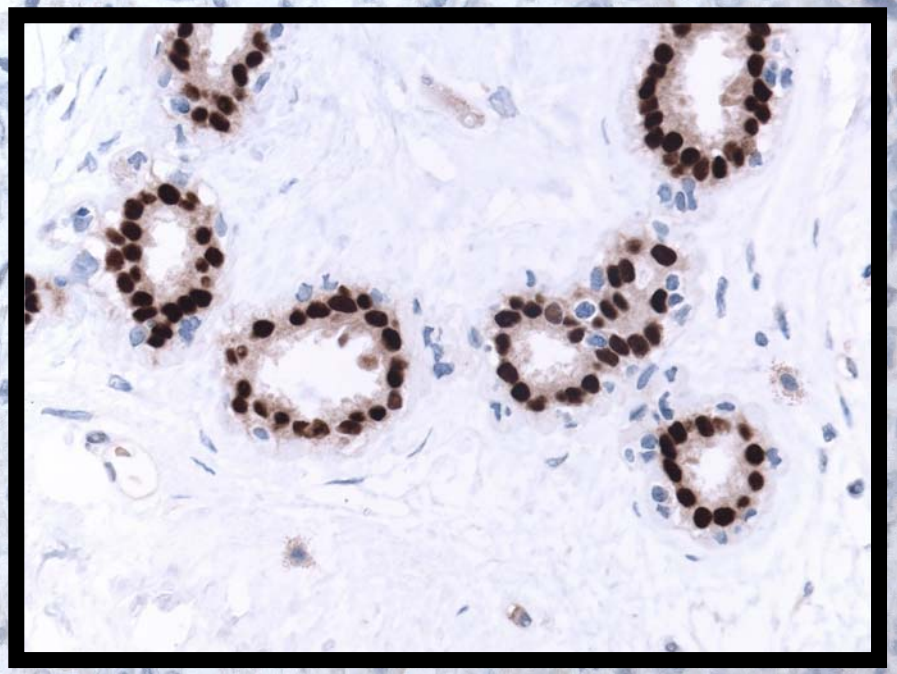
ER and PR

- ER/PR
  - DCC method
  - IHC all or none method
  - IHC, Allred score
  - Image analysis

Fisher E, et al, Cancer 2004

ER and PR

- Quality control
- Quality assurance



ER and PR

Mount Sinai Hospital

- Fix in 10% neutral buffered formalin for 8-24 hours, following slicing to allow adequate fixation
- Baylor abs and method:
  - ER, 6F11: PgR,1294
- Allred scoring system

ER and PR

Mount Sinai Hospital

Reporting

% positive tumor nuclei	Classification
0	Negative
1-9%	Low positive
10-100%	Positive

CAP consensus, 2000: Goldhirsch et al, 2001: NIH consensus document, 2000

Immunohistochemical Studies:

Estrogen Receptor Protein:

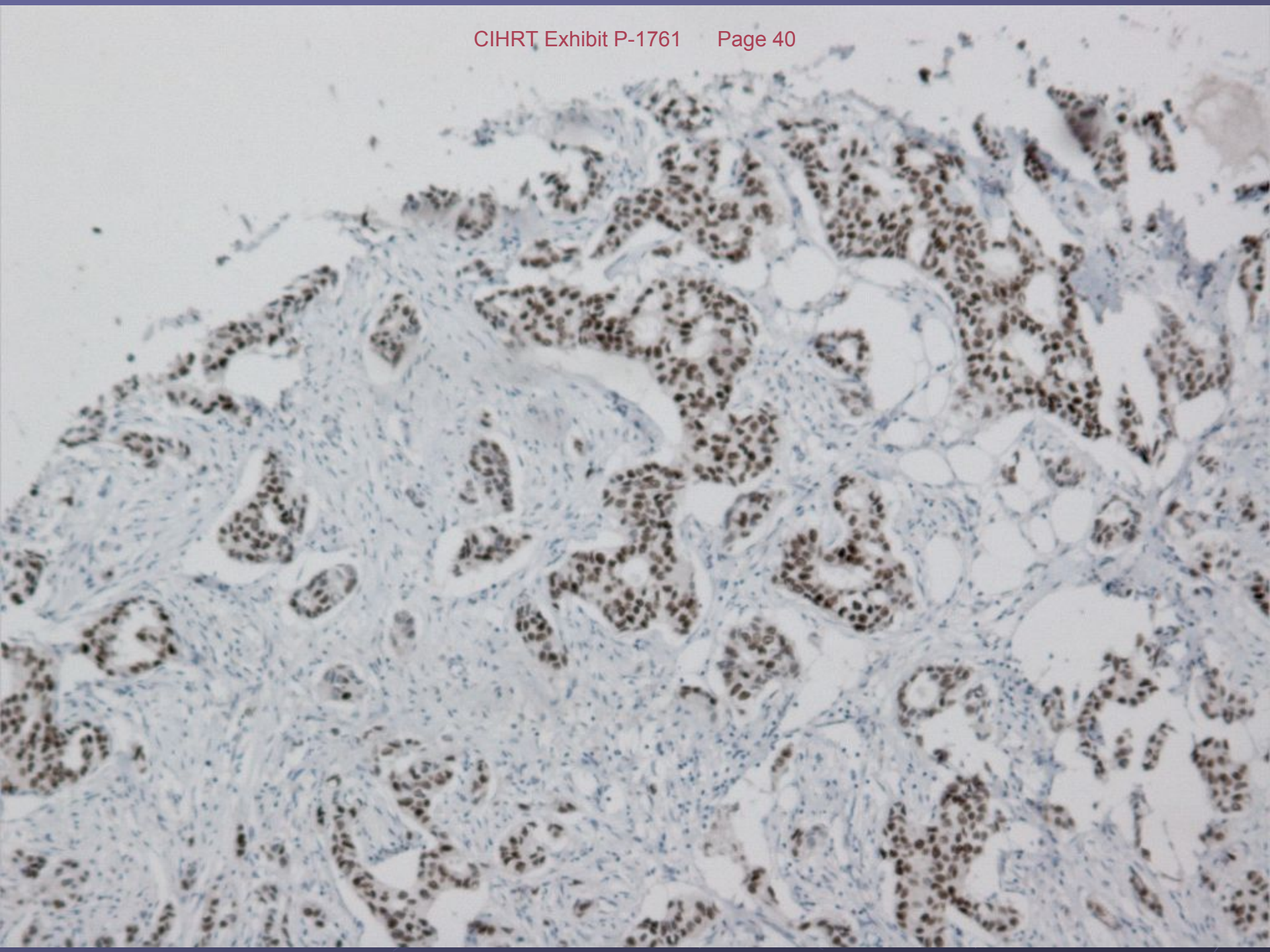
- % positive cells: > 90%
- Antibody used: 6F11, LSAB procedure

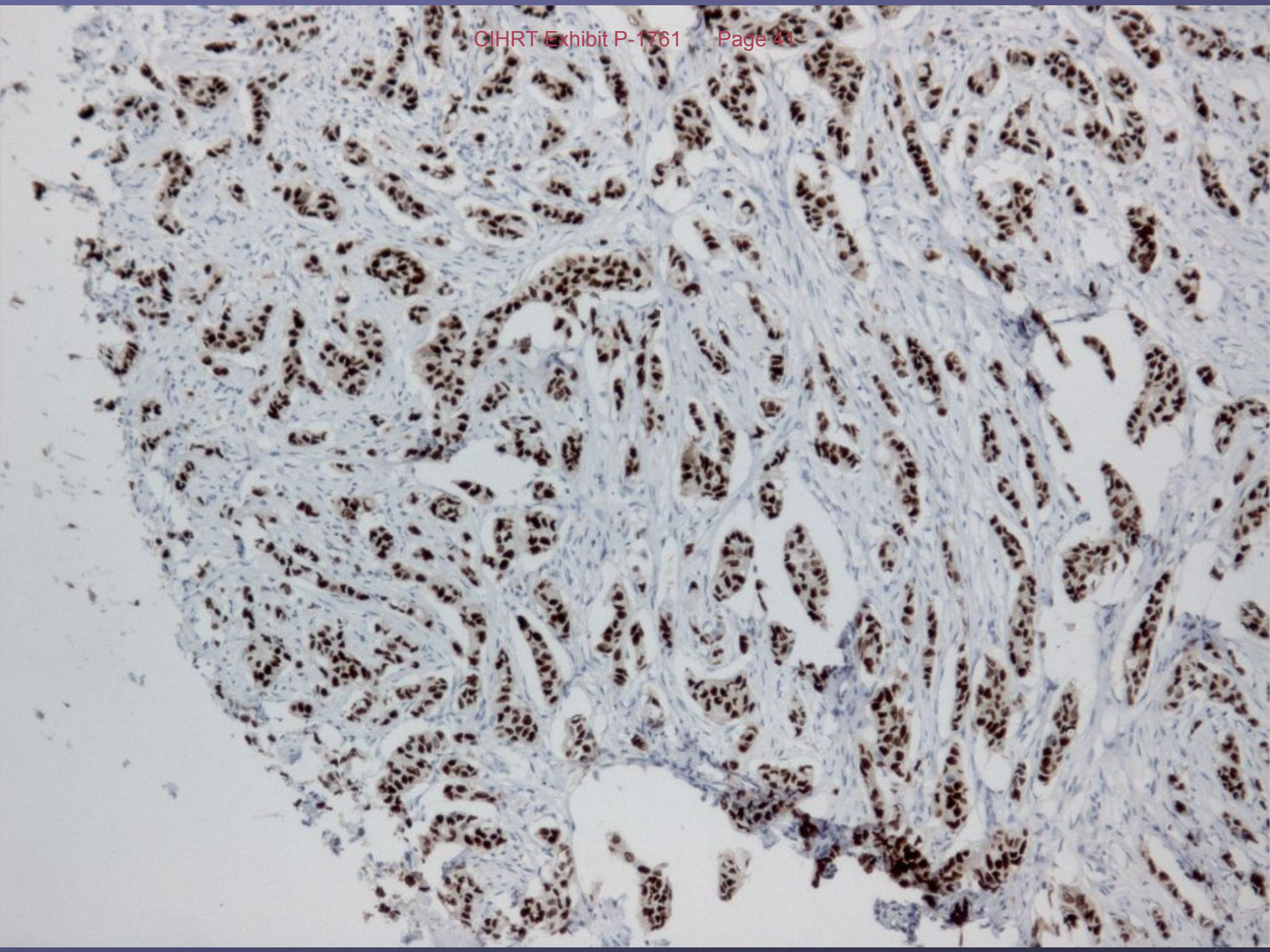
Progesterone Receptor Protein:

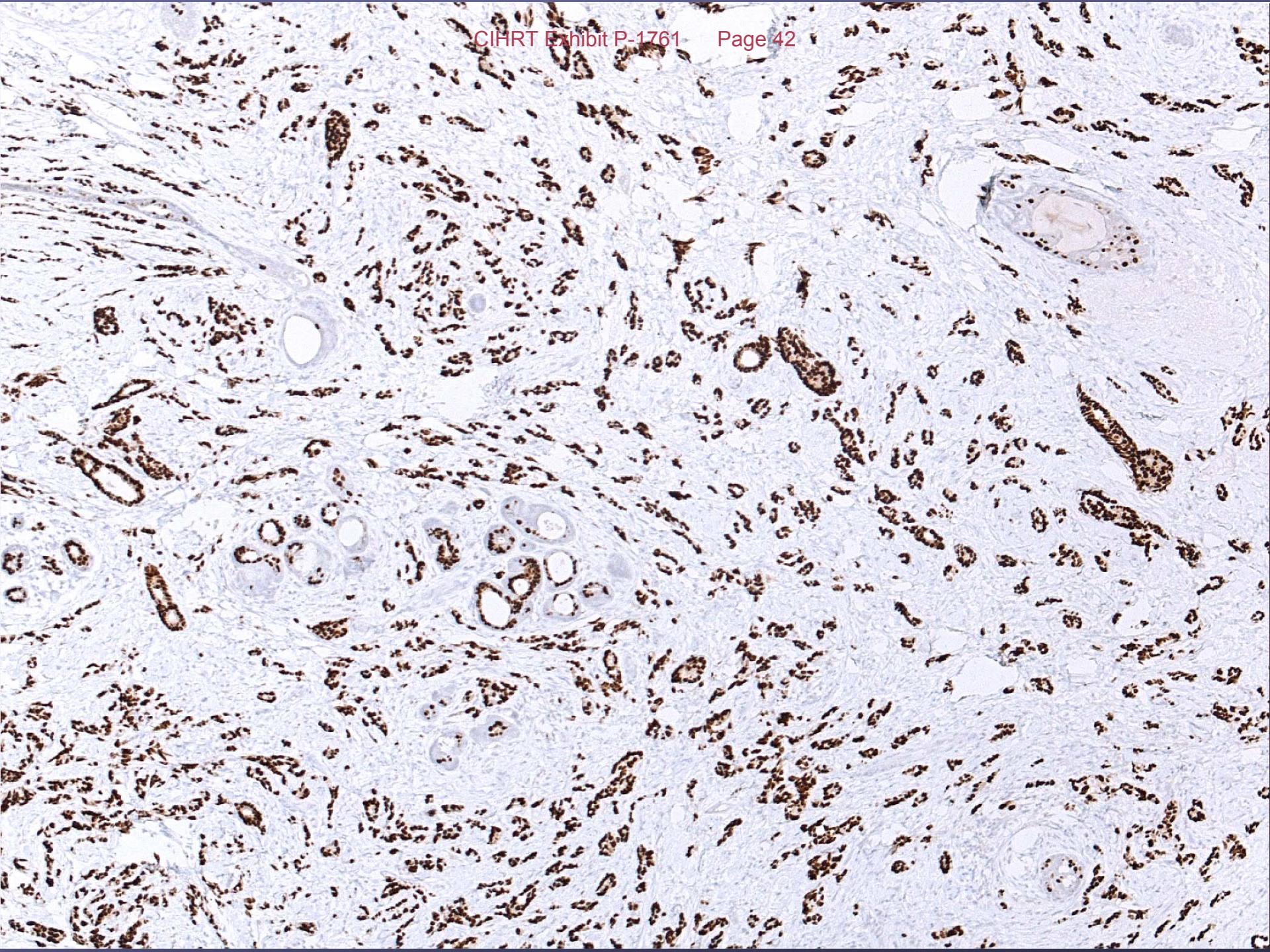
- % positive cells: Approx 60%
- Antibody used: PGR 1294, LSAB procedure

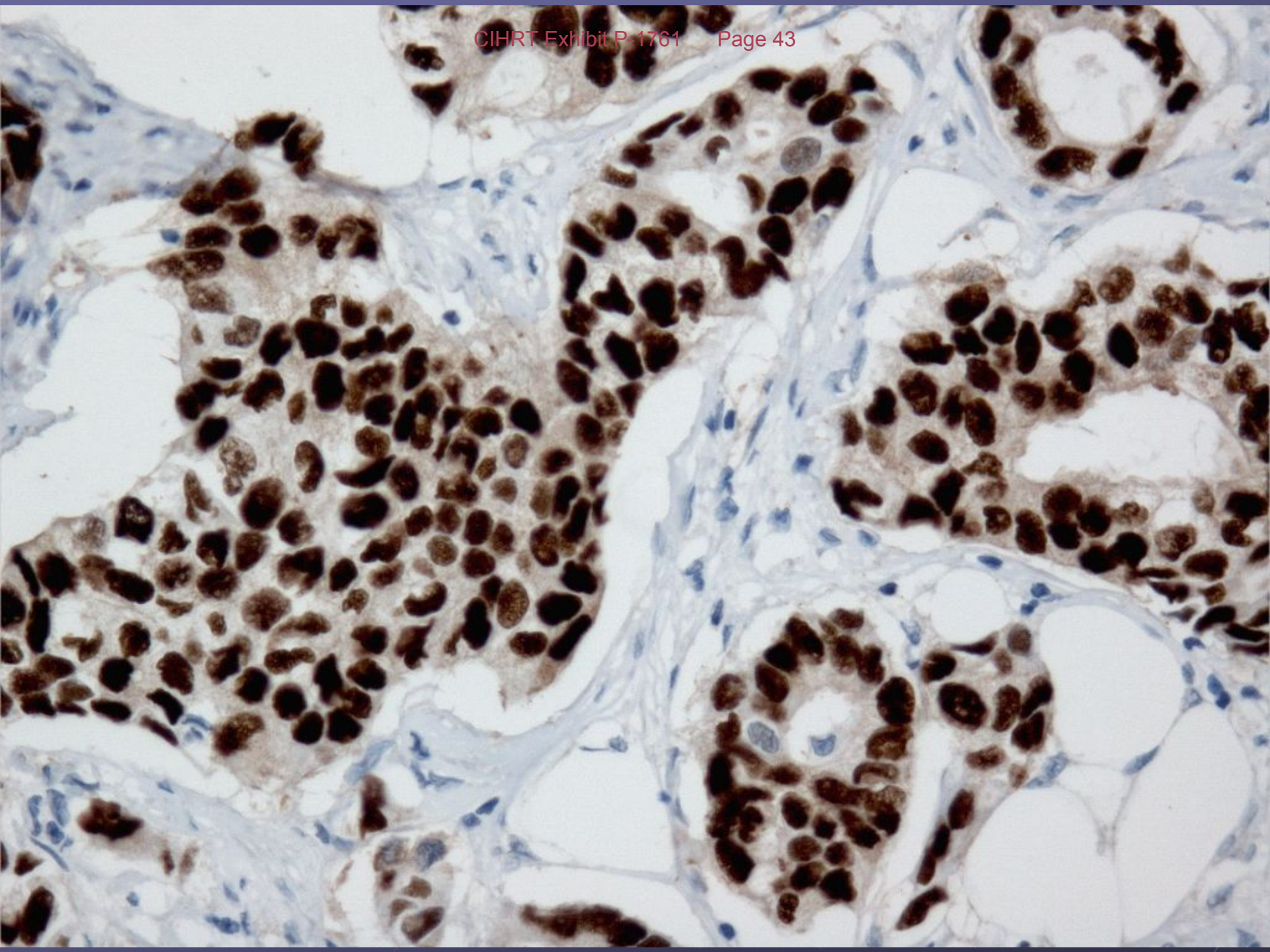
Positive and negative laboratory controls stained appropriately

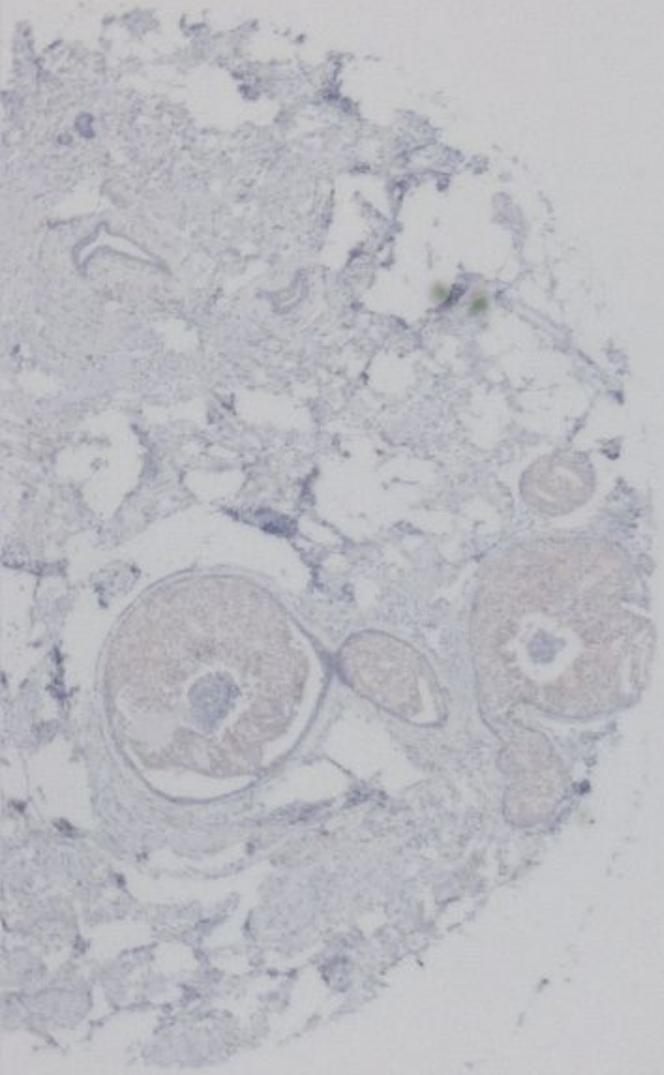
THRESHOLD FOR POSITIVE ER/PR RESULT: > 1% nuclear positivity of tumour cells (Harvey et al, JCO 17:1474-1481, 1999)

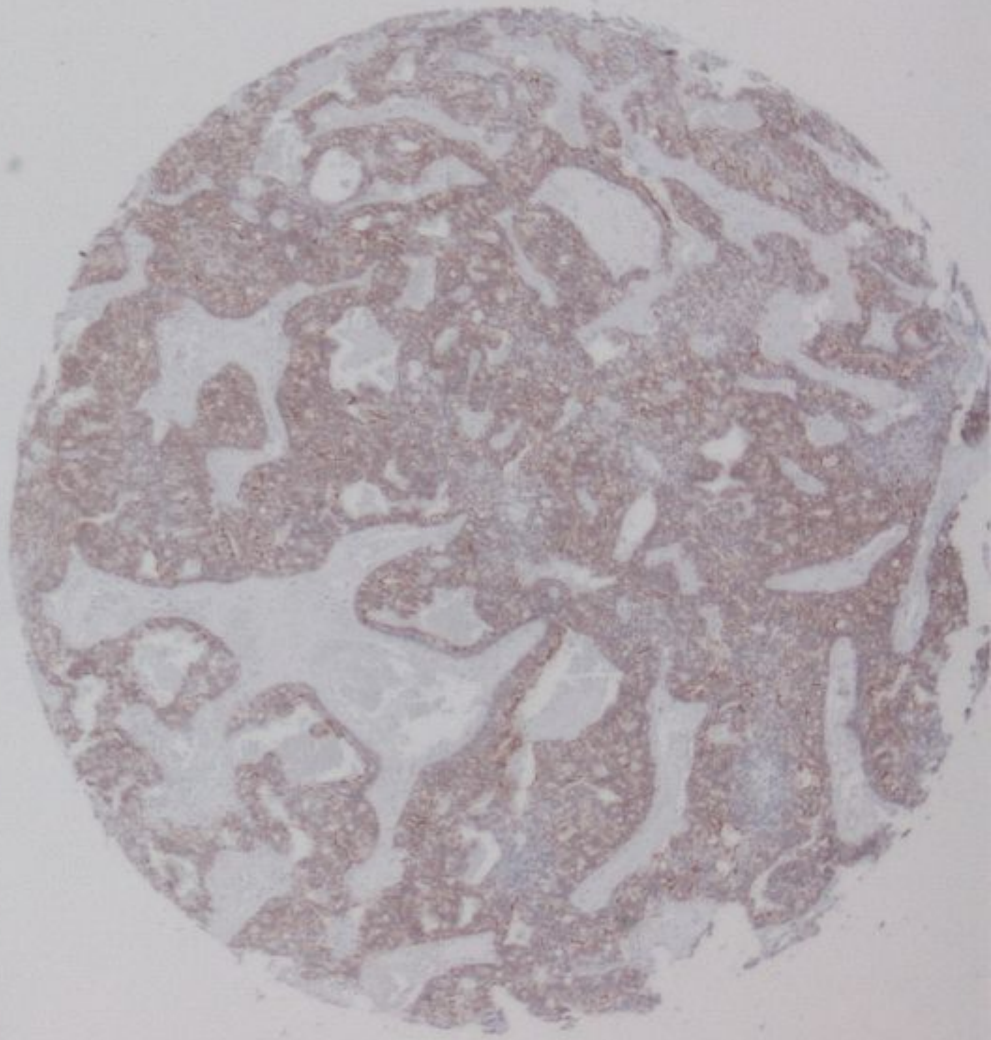


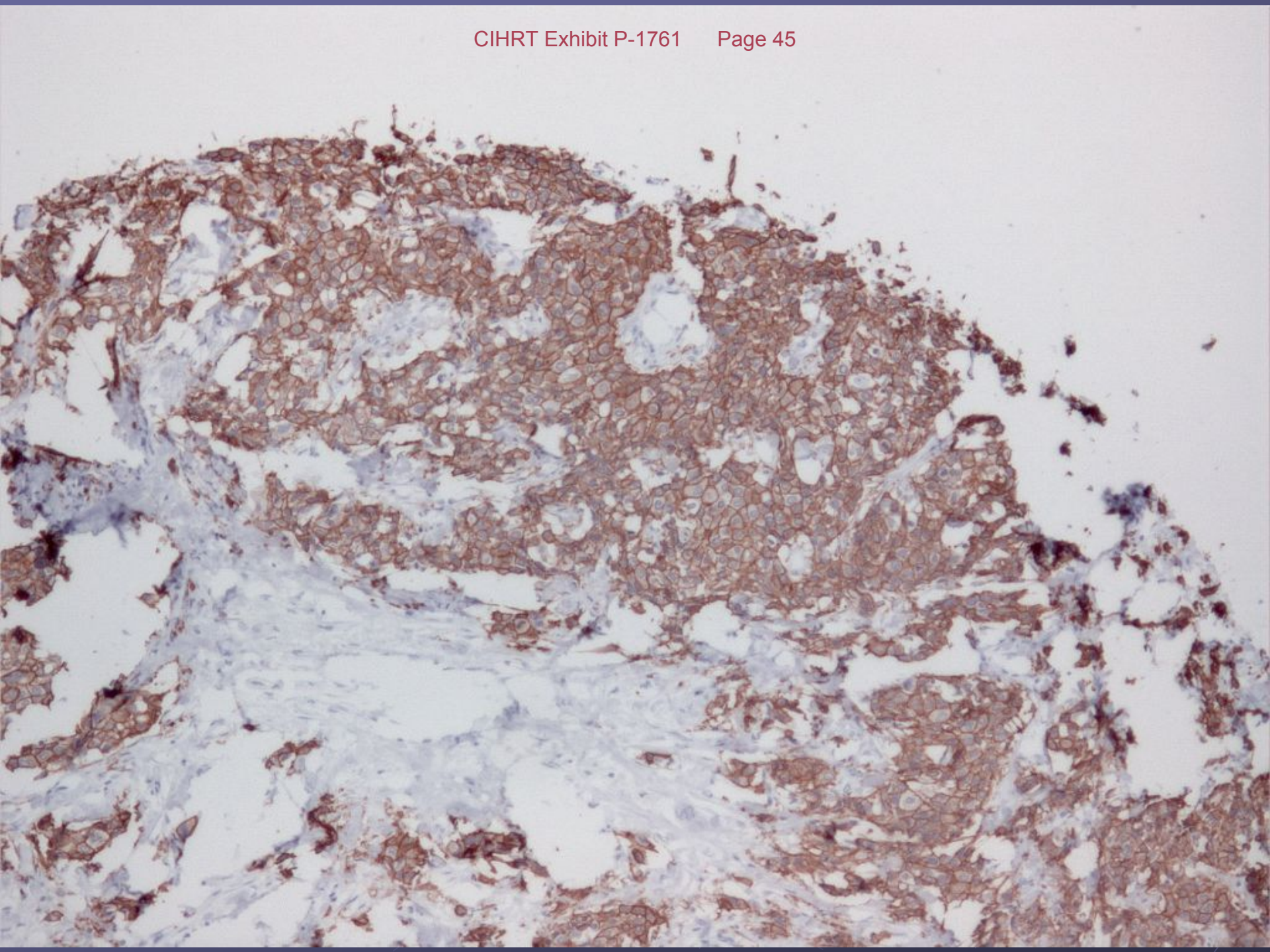


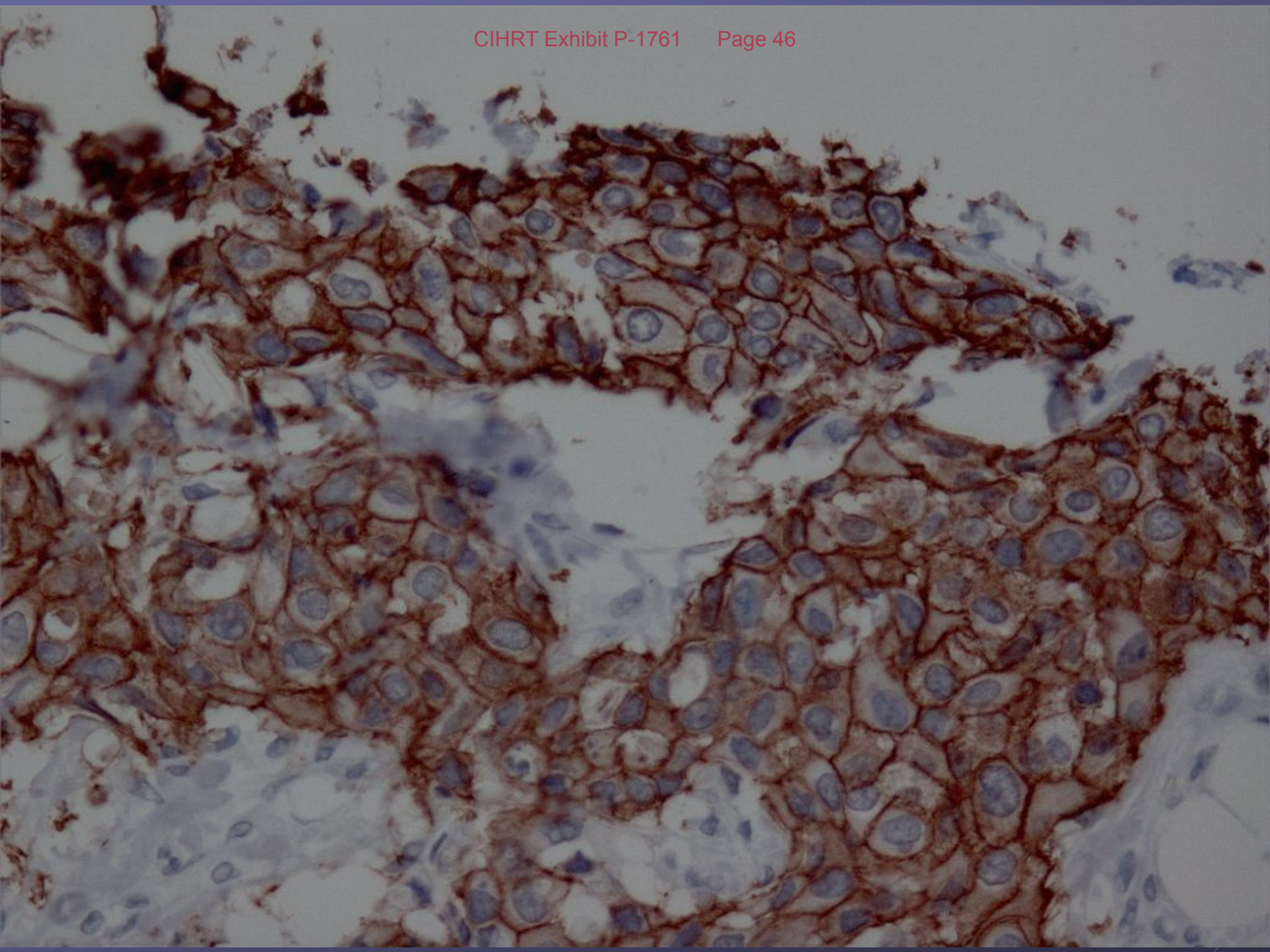


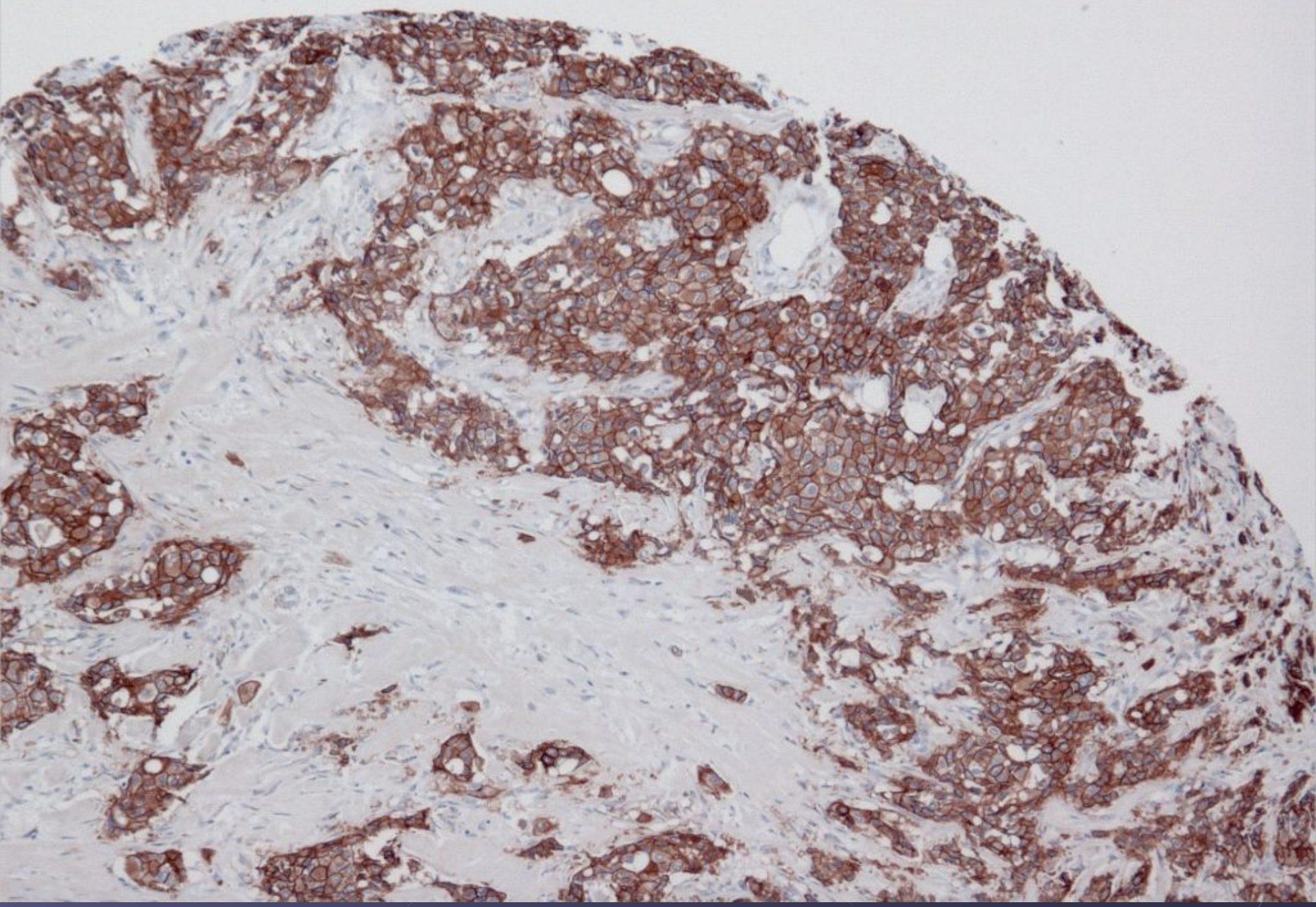


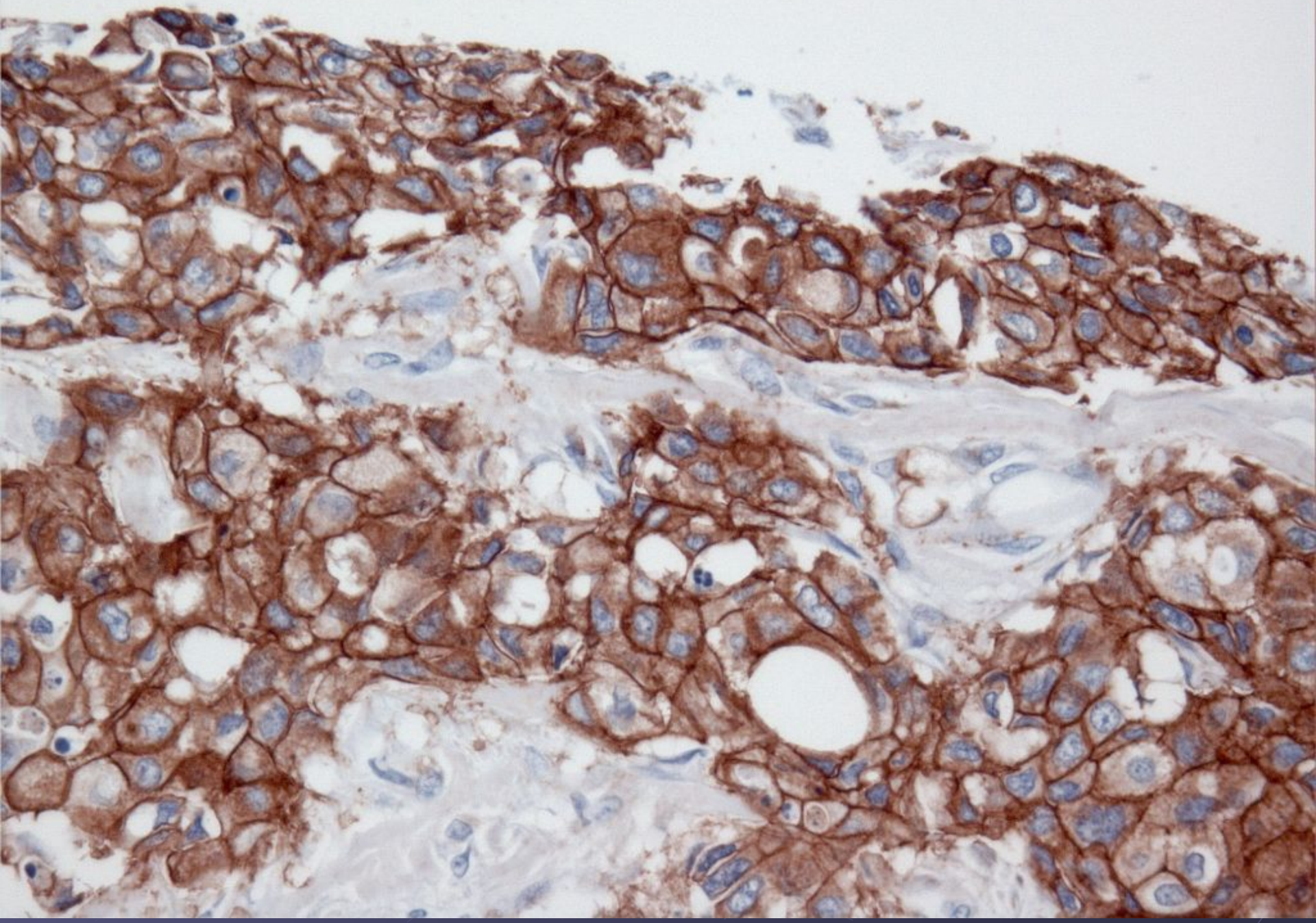












When I got home last night,
I wanted to go out to some place expensive.....

So I went to the gas station