

SYNCHROTRON BASED

FTIR SPECTROSCOPY.

WHAT DOES THE CLINICIAN NEED?

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NHS

NHS Trust

- **Cancer diagnosis.**
- **Standardisation.**
- **Validation.**
- **The way forward.**

WHY CANCER?

- **High incidence.**
- **One of the main causes of death.**
- **Socio-economic impact.**
- **Management of cancer patients needs improving.**

Figure 1.1: The 20 most commonly diagnosed cancers (ex NMSC), UK, 2004

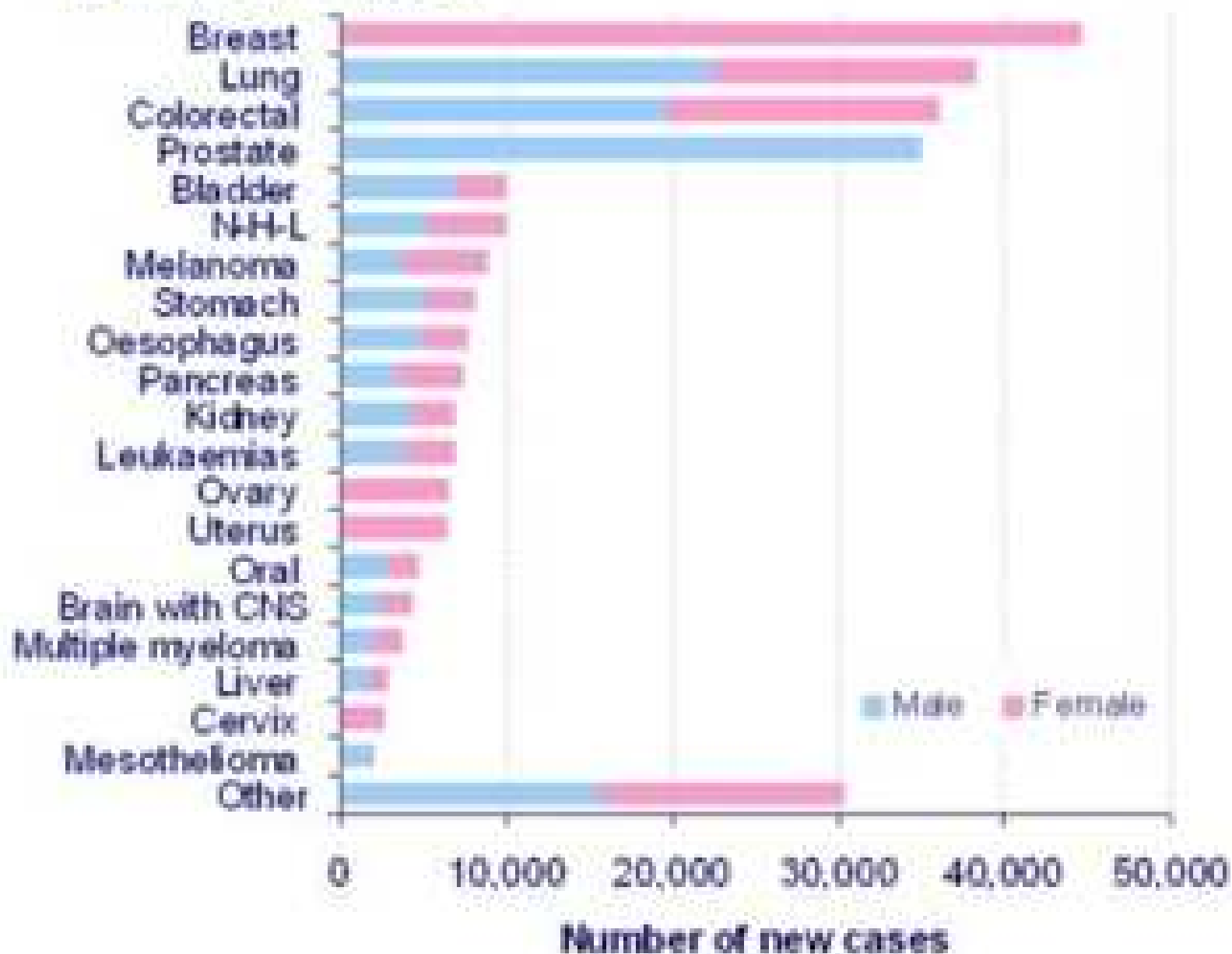
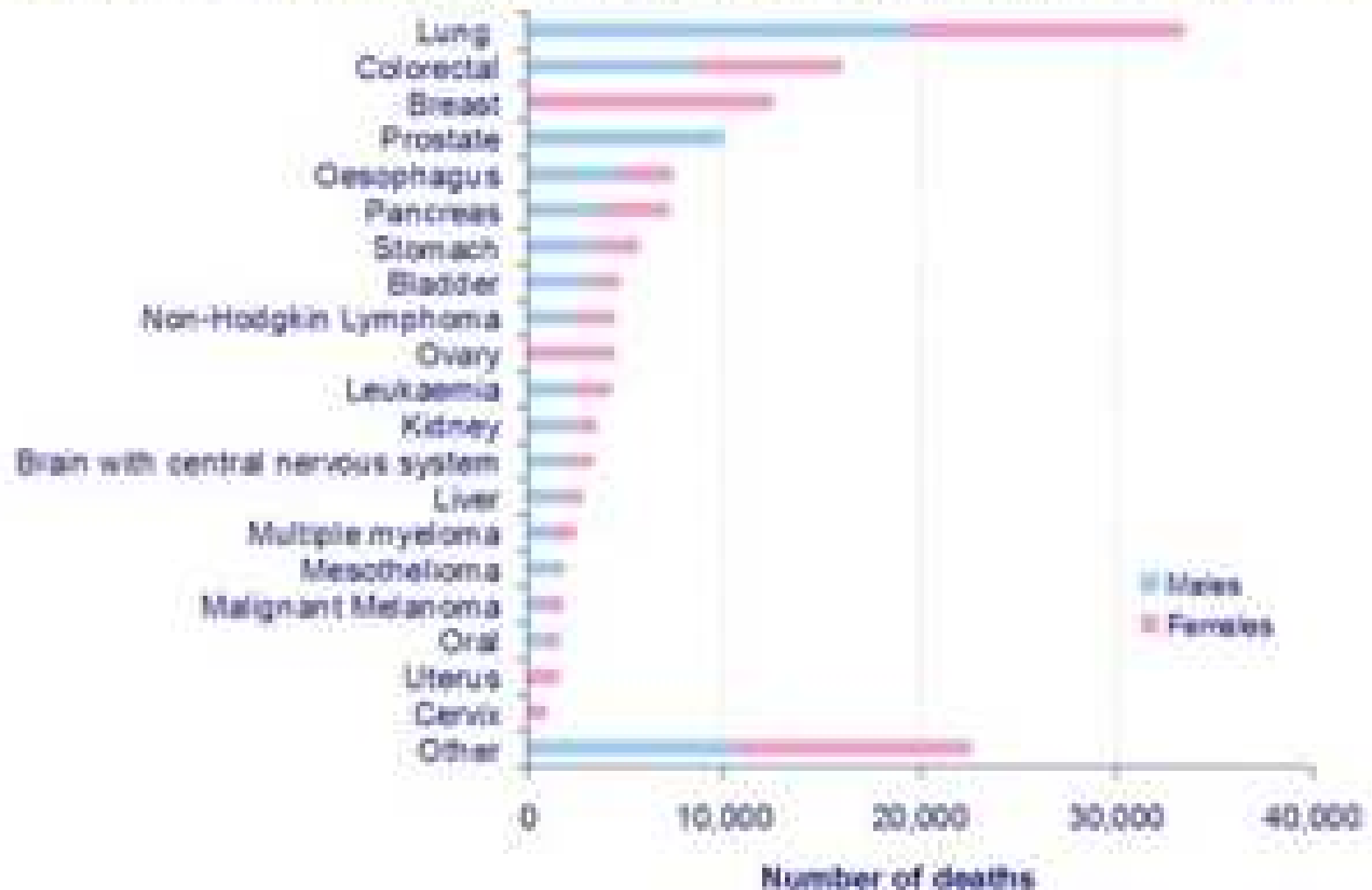


Figure 1.1: The 20 most common causes of death from cancer, UK, 2005

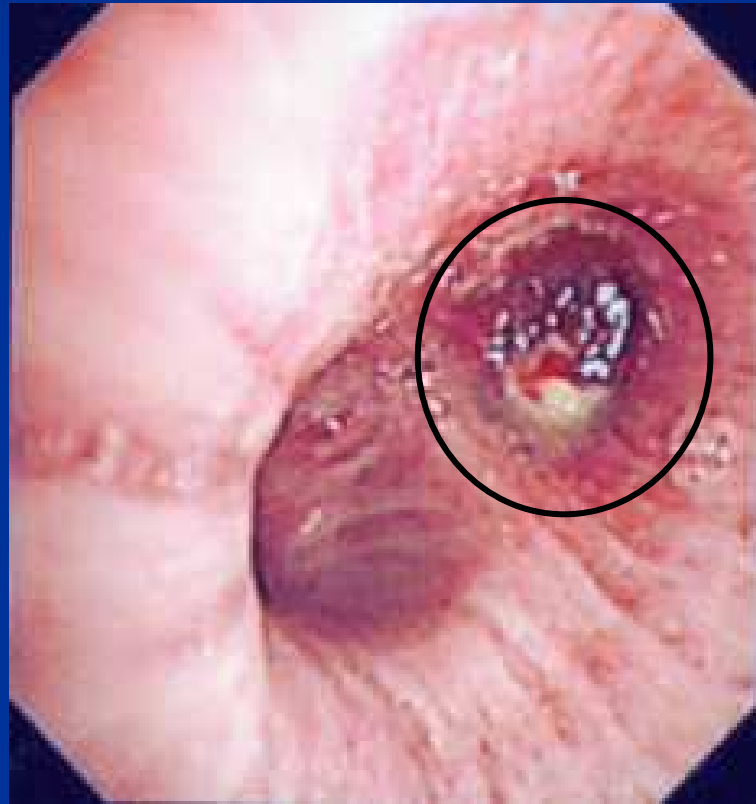


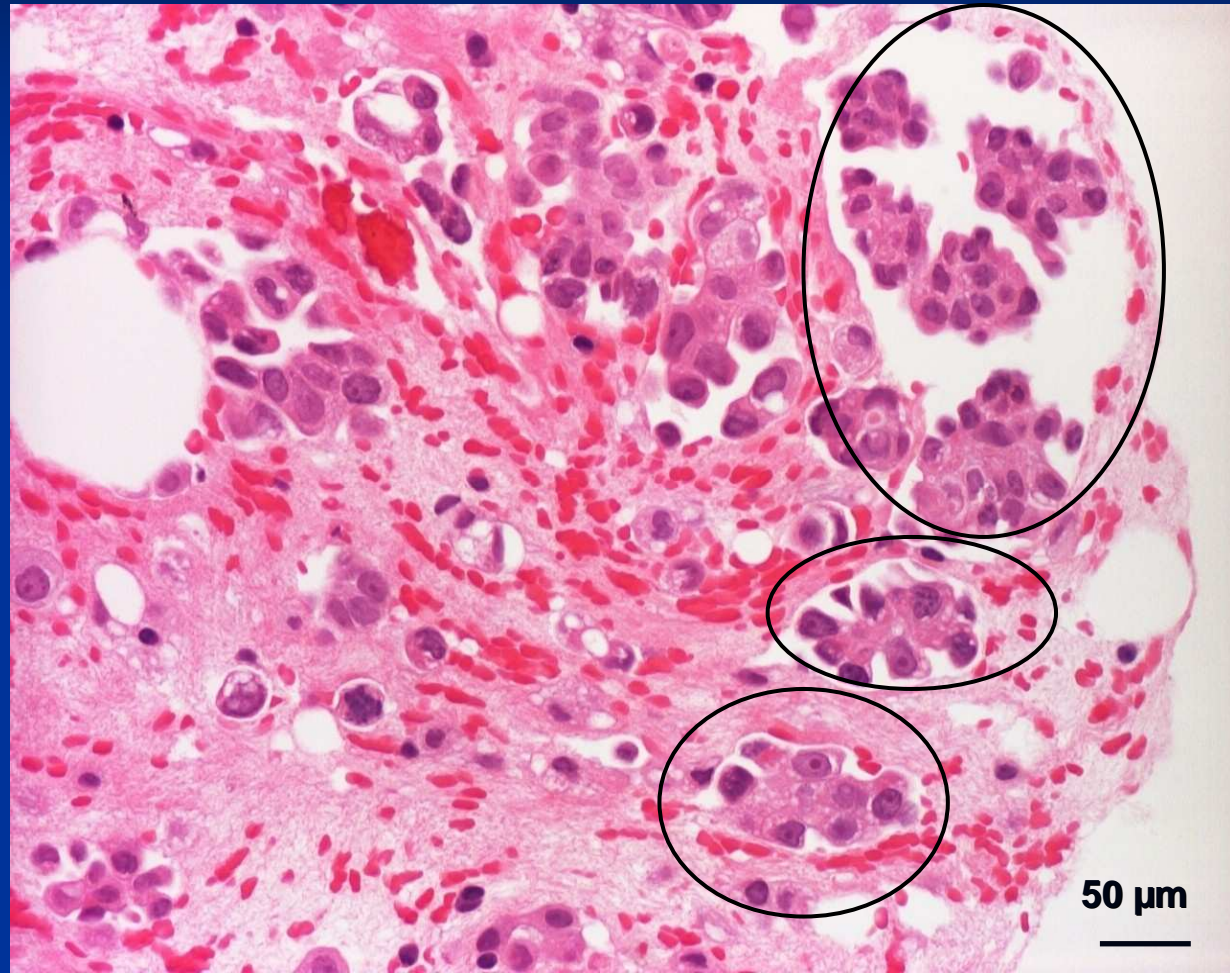
WHY SYNCHROTRON?

- **Rapid data acquisition.**
- **Minimal sample preparation.**
- **Non destructive.**
- **To study cells at single and subcellular level.**

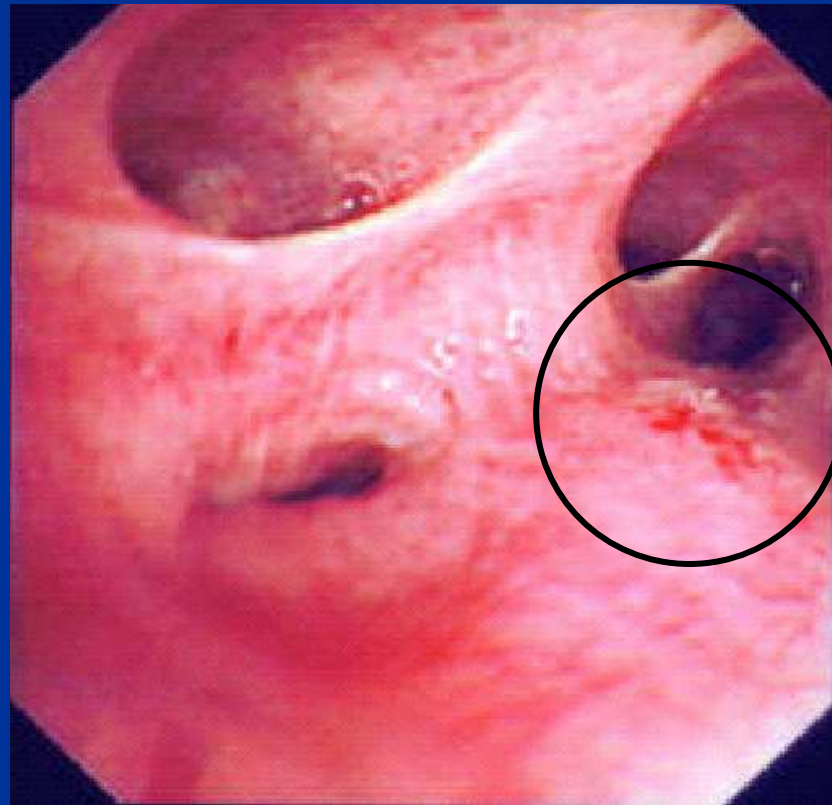
HISTOLOGICAL DIAGNOSIS OF CANCER

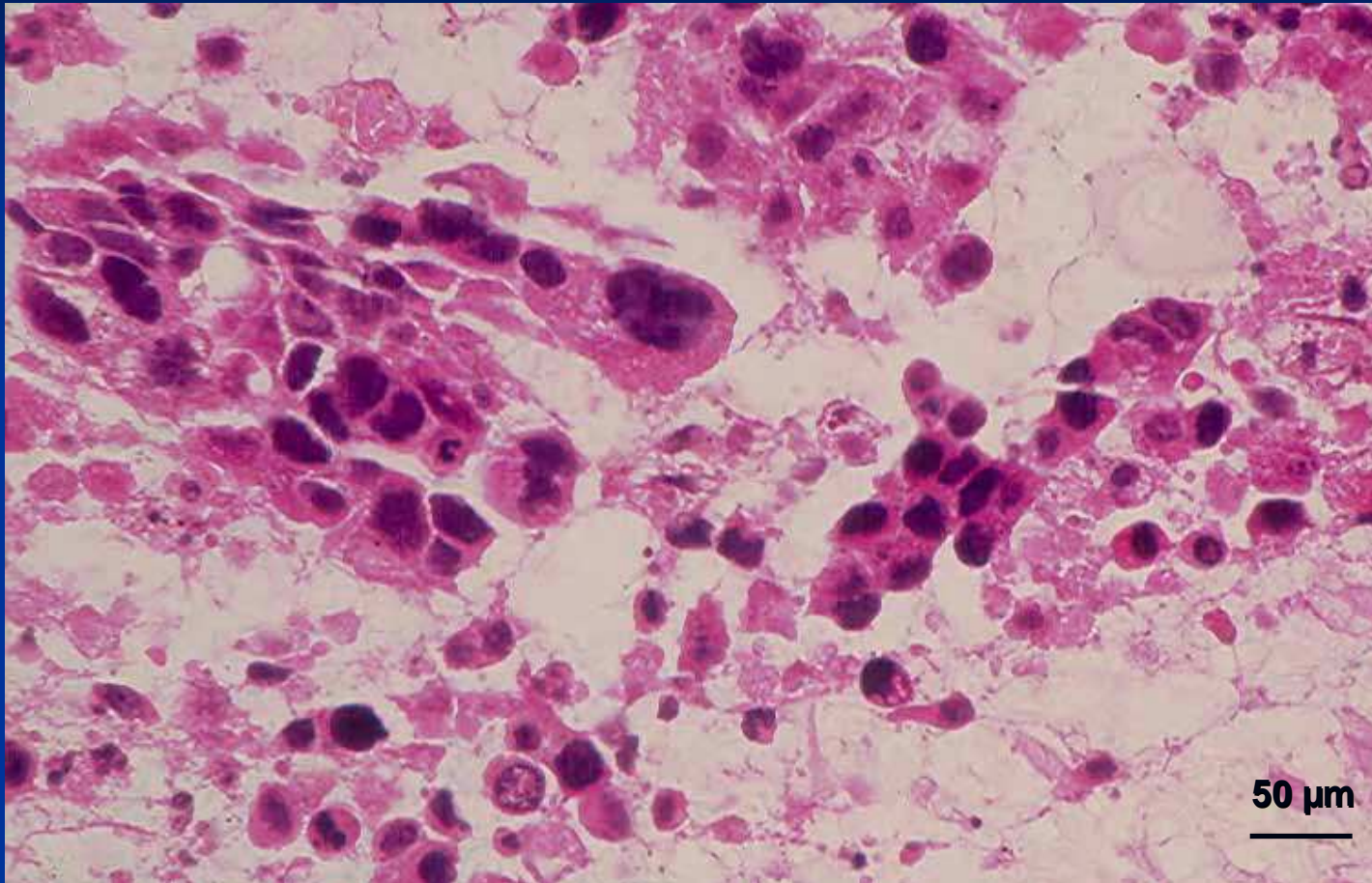
BRONCHOSCOPY IMAGE OF A LUNG TUMOUR





BRONCHOSCOPY IMAGE OF A LUNG TUMOUR





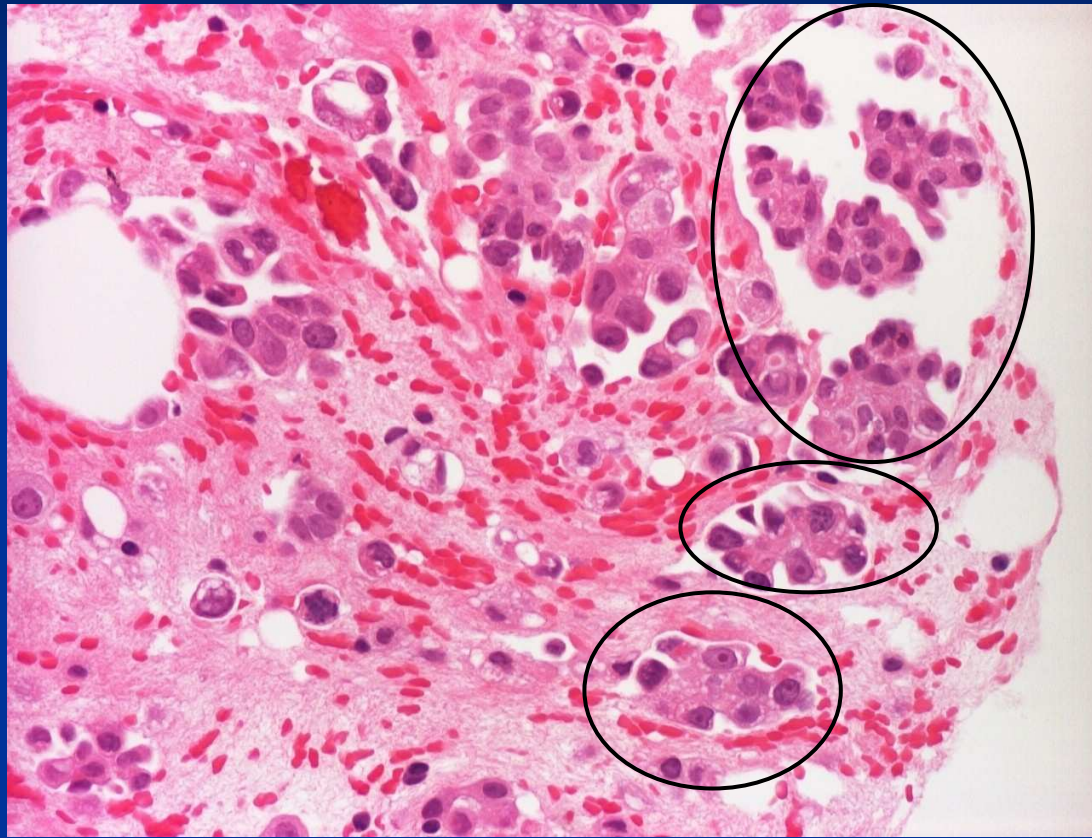
Squamous carcinoma

APPLICATION IN HISTOLOGY

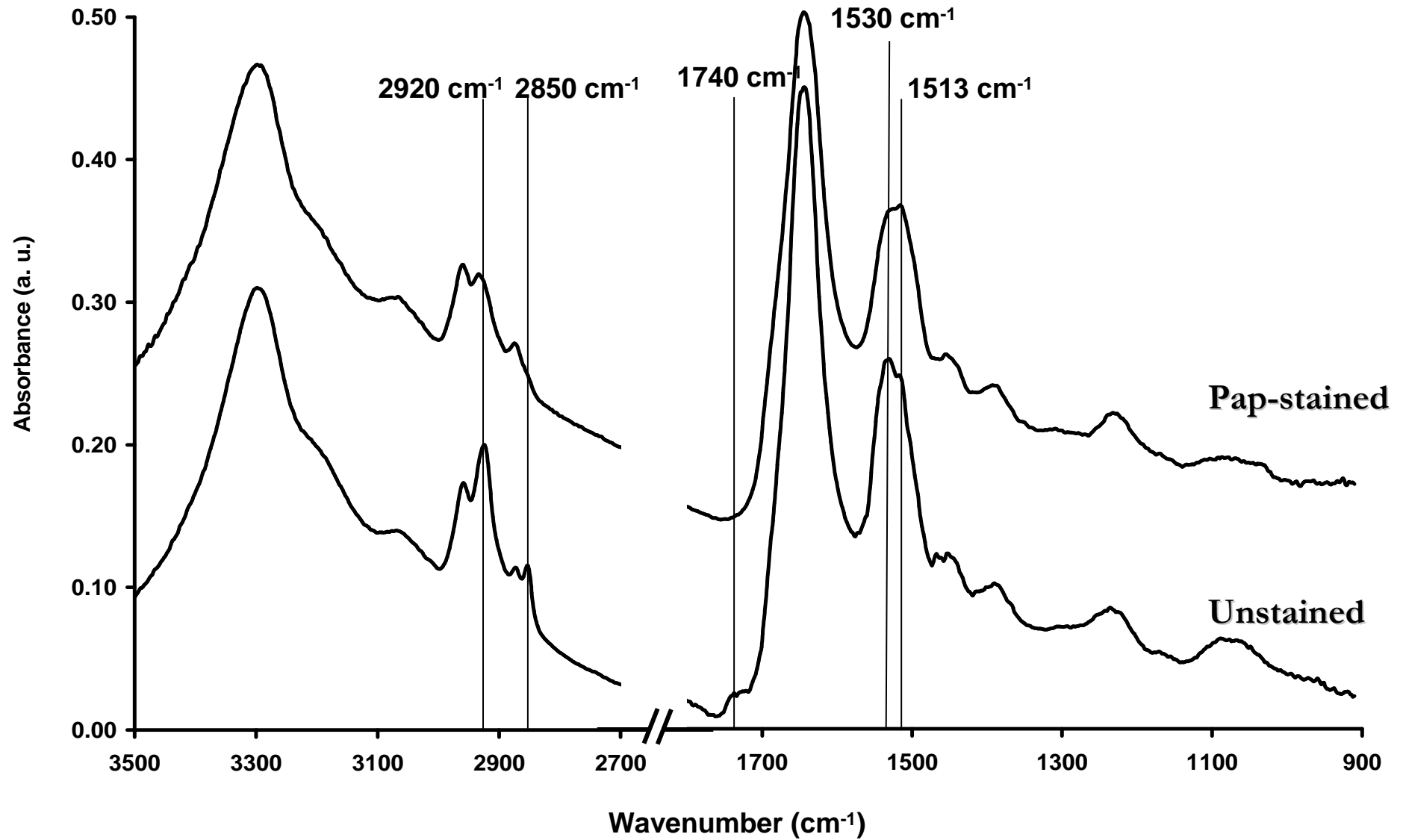
- **Screening:**
 - **Tissue samples.**
 - **Cytology samples.**
- **Diagnosis at single cell level.**

MEDICAL APPLICATIONS

- **Screening:**
 - Tissue samples.
 - Cytology samples.
- **Diagnosis at single cell level.**



CALU-1 LUNG CANCER CELLS



Pijanka J., et al. Lab Invest 90: 797-807; 2010.

TISSUE SAMPLE

- Is it normal?
- Is it tumour?
- Which type of tumour is it?

IS IT NORMAL?

Eckel R.	Vibrat Spec, 2001.	Breast v fibroadenoma.
Wood B. R.	Gynecol Oncol, 2004	Cervix v dysplasia
Li Q.-B.	Clin Chem, 2005	Stomach and gastritis
Murali K. C.	Anal Bioanal Chem, 2007	Ovary
Walsh M. J.	Biochem Biophys Res Comm, 2007	Cervix v dysplasia
Quaroni L.	Analyst, 2009	Oesophagus v Barrett

IS IT TUMOUR?

Yano K.	Anal Biochem, 2000	Lung
Eckel R.	Vibrat Spec, 2001	Breast
Salman A.	Cell Mol Biol, 2001	Colon
Neviliappan S.	Gynecol Oncol, 2002.	Cervix
Argov S. J	Biomed Optics, 2002.	Colon
Lasch P.	Technol Cancer Res Treat, 2002.	Colon, prostate
Fabian H. J	Mol Struct, 2003.	Breast
Gazi E.	J Pathol, 2003.	Prostate
Malins D. C.	PNAS, 2003	Prostate
Mordechai S.	J Microsc, 2003	Cervix, melanoma
Ramesh J.	J Lab Clin Med, 2003.	Leukaemia
Wang J.-S.	World J Gastroenterol, 2003,	Oesophagus
Li Q.-B.	Clin Chem, 2005	Stomach
Sahu R. K. J.	Biomed Optics, 2005	Colon, cervix
Krafft C.	Anal Bioanal Chem, 2007	Brain
Paluszkiewicz C.	Vibrat Spectrosc, 2007	Prostate
Kelly J. G.	Cancer Lett, 2009	Endometrium
Harvey T. J.	Analyst, 2009	Prostate
Bird B.	J. Biophoton, 2010	Lymph node

WHICH TYPE OF TUMOUR IS IT?

Steiner G.

Biopolymers, 2003.

Glioma grades

Krafft C.

Technol Cancer Res Treat, 2006.

Types of metastases

Babrah J.

Analyst, 2009.

Leukaemia

MALIGNANT TUMOURS IN LUNG

- Squamous cell carcinoma
- Adenocarcinoma
- Adenosquamous
- Large cell carcinoma
- Bronchio-alveolar carcinoma
- Small cell carcinoma
- Pleomorphic, sarcomatoid or sarcomatous tumours
- Carcinoid tumours
- Carcinomas of salivary gland type
- Unclassified
- Metastases (breast, bowel, stomach, kidney, thyroid, ovary, ...)

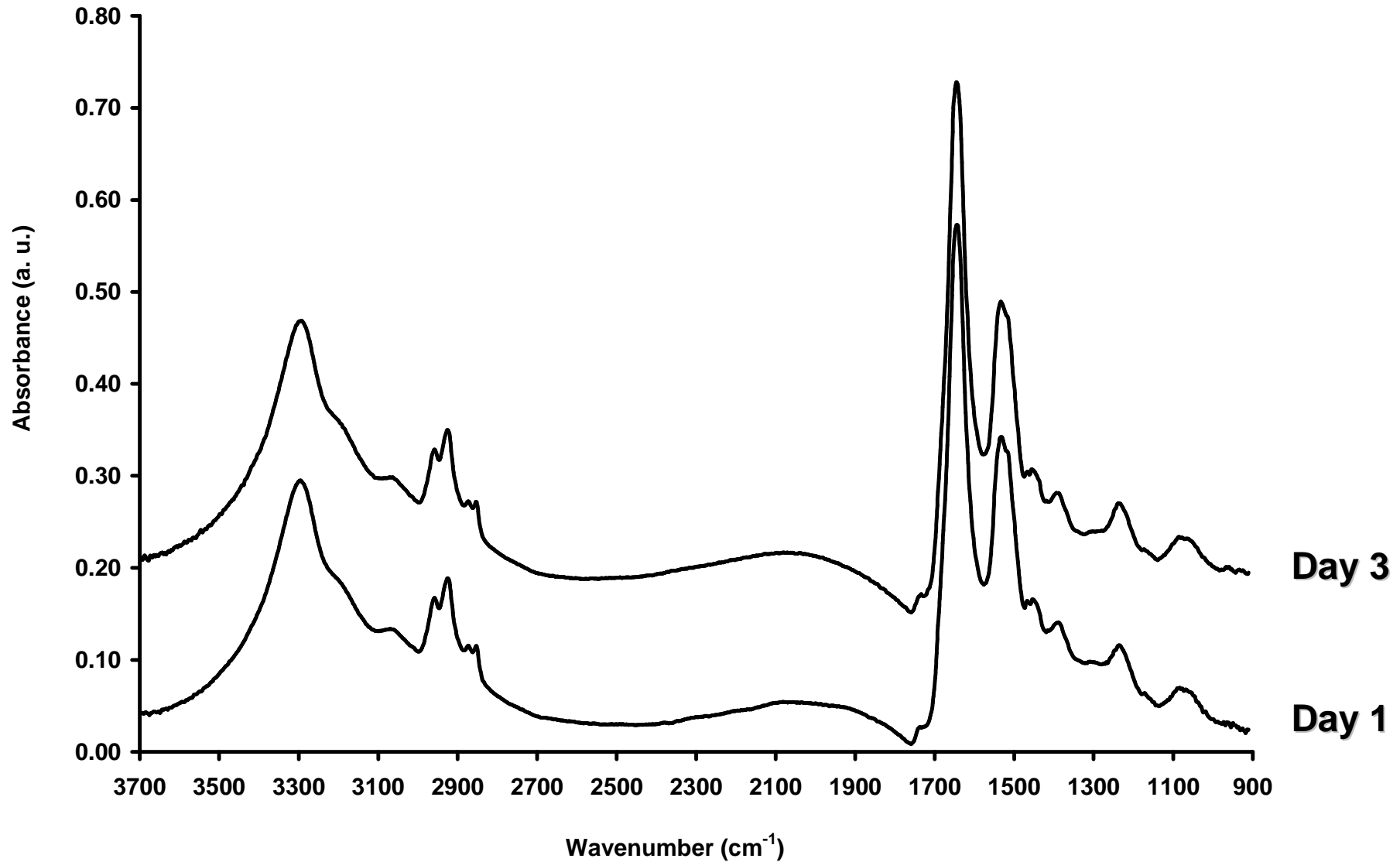
FTIR SPECTROSCOPY AND CANCER DIAGNOSIS

- Cancer diagnosis.
- **Standardisation.**
- Validation.
- The way forward.

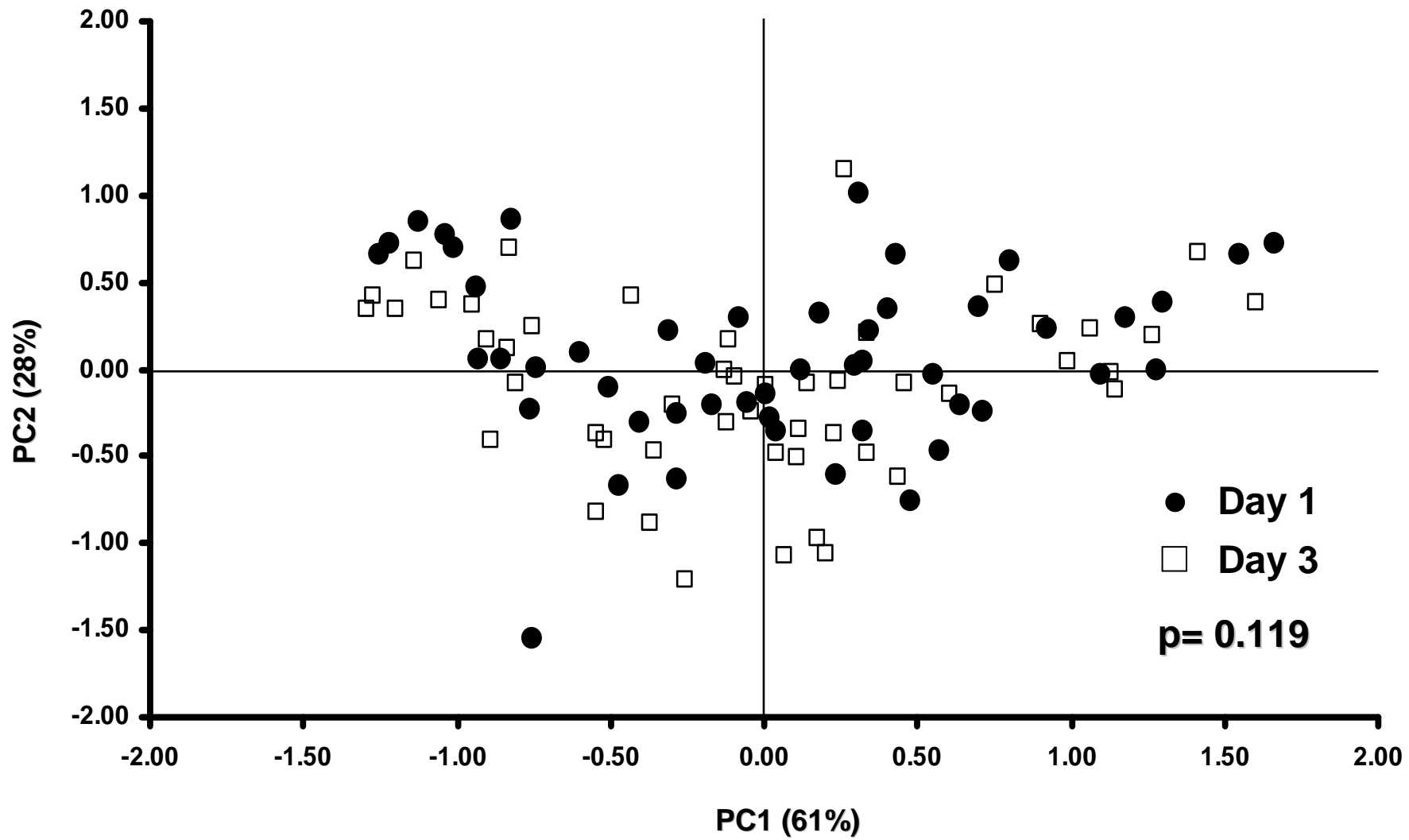
STANDARDISATION

- **Sample preparation.**
- **Data collection (reflectance, transmission).**
- **Data correction, analysis and statistics.**
- **Same results obtained at:**
 - **Different centres (synchrotrons).**
 - **Same and different spectrometers.**
 - **Different time points.**

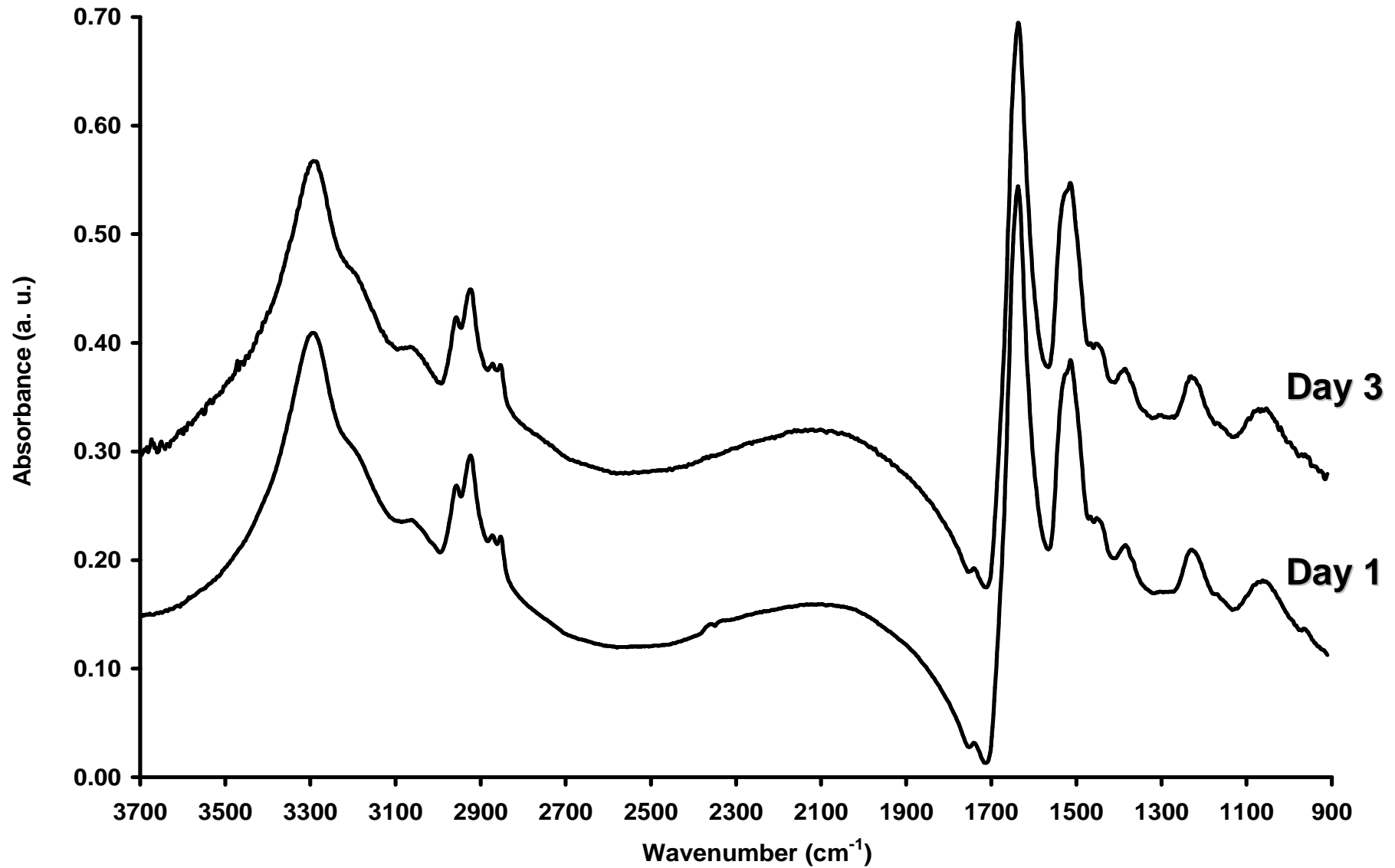
CALU-1 LUNG CANCER CELLS



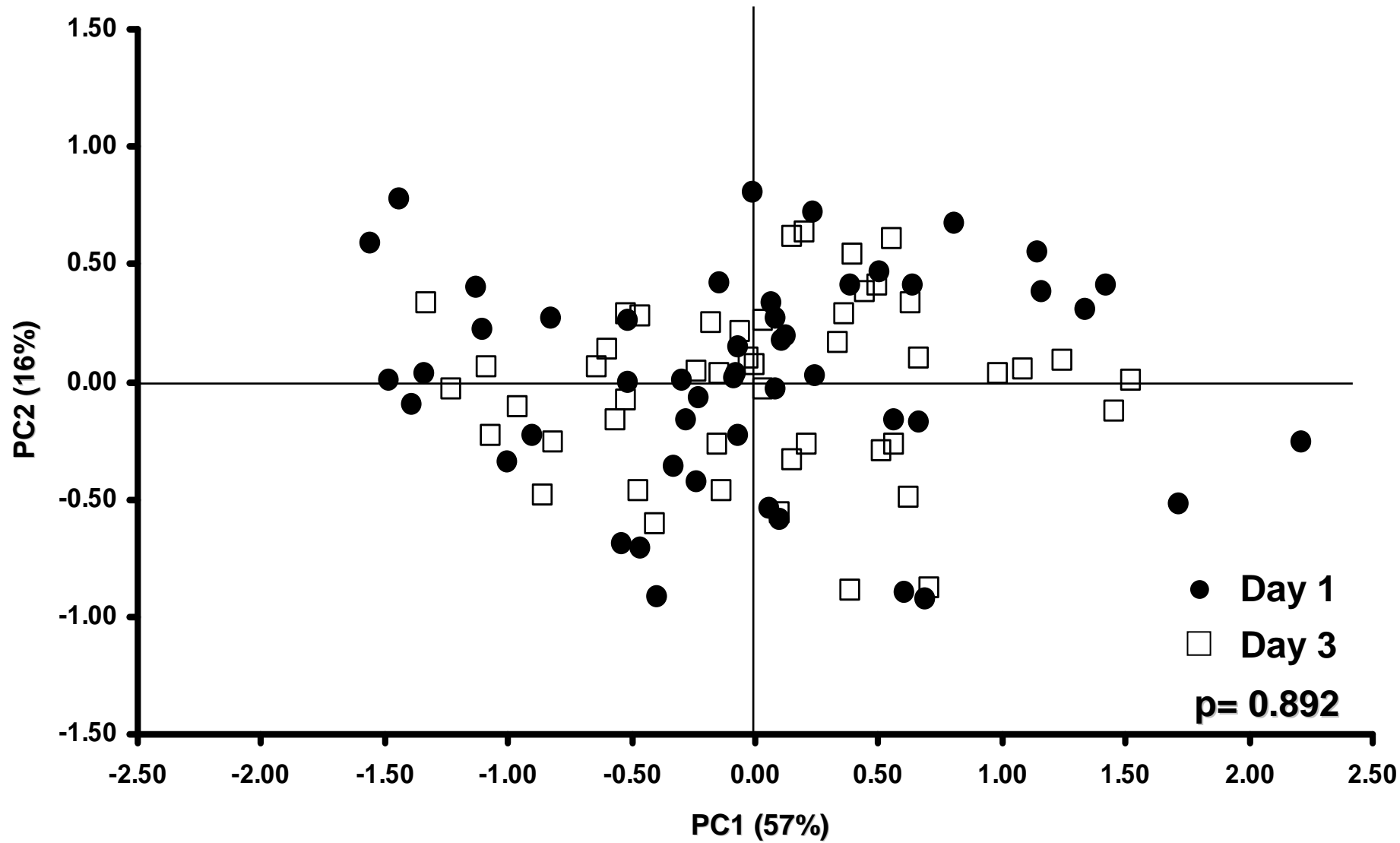
Pijanka J., et al. Lab Invest 90: 797-807; 2010.



NL20 LUNG EPITHELIAL CELLS



Pijanka J., et al. Lab Invest 90: 797-807; 2010.



FTIR SPECTROSCOPY AND CANCER DIAGNOSIS

- Cancer diagnosis.
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- **Validation.**
- The way forward.

VALIDATION

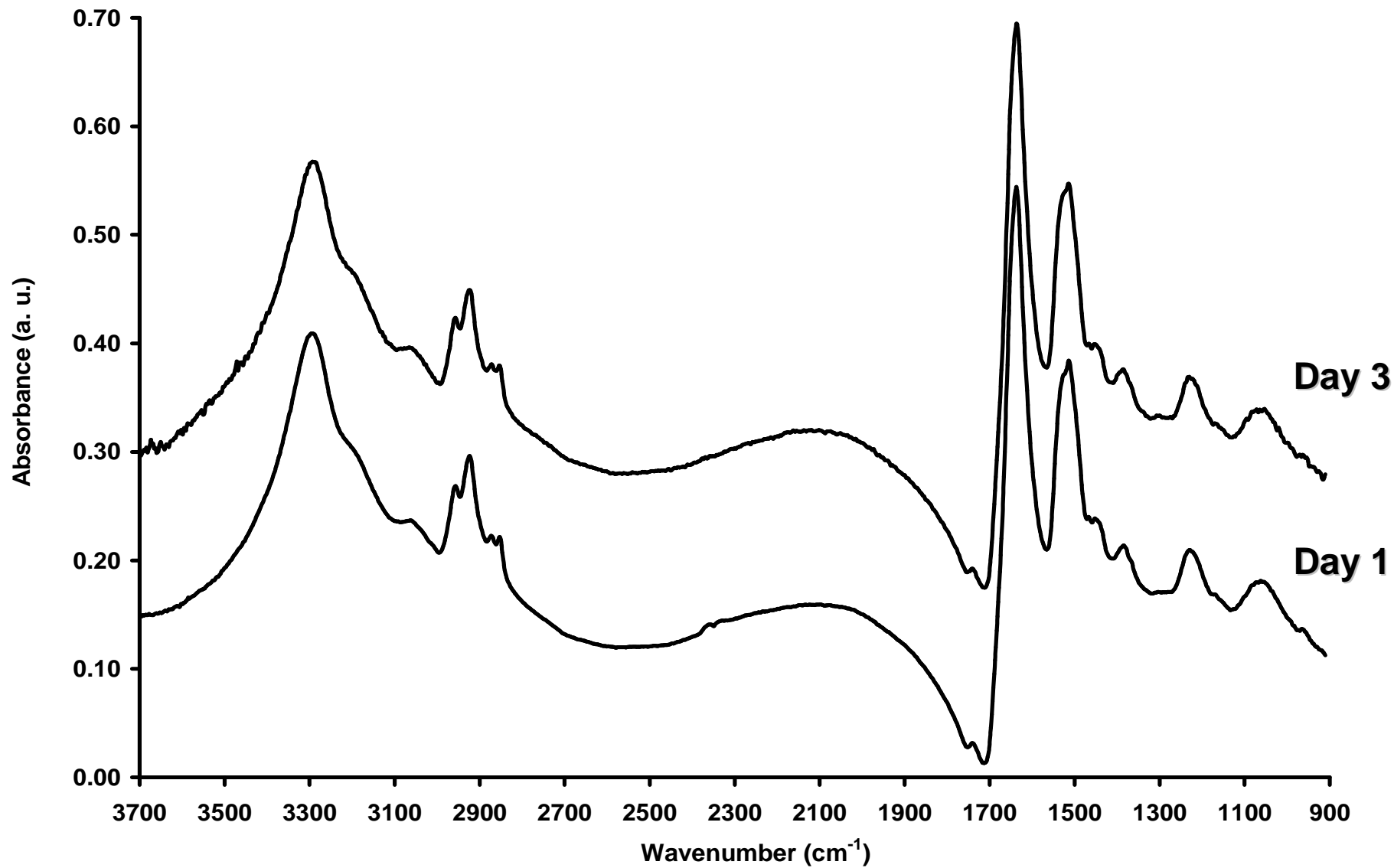
THE DATA OBTAINED WITH

FTIR SPECTROSCOPY

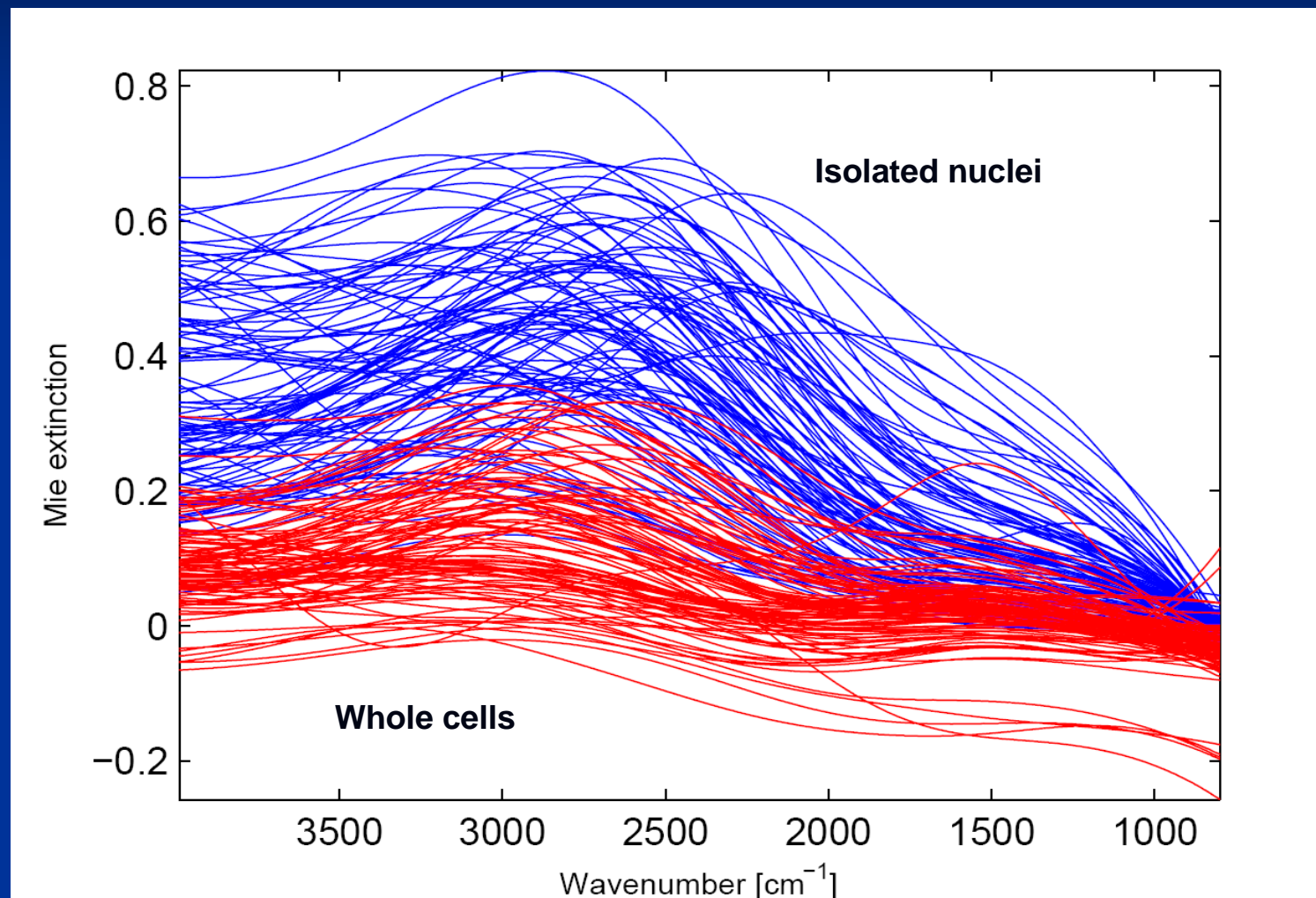
NEEDS TO BE VALIDATED

WITH OTHER STANDARD TECHNIQUES

NL20 LUNG EPITHELIAL CELLS



MIE SCATTERING CURVES



- Kohler A., Sulé-Suso J., Sockalingum G. D., *et al.* Appl Spectrosc 62: 259-266; 2008.
- Bassan P., *et al.* Analyst 134: 1586–1593; 2009.
- Bassan P., *et al.* Analyst 135: 268–277; 2010.
- Bird B., *et al.* Biophoton. 3, No. 8–9, 597–608; 2010.

CANCER CELLS' NUCLEI

Changes in nuclear shape

- Malleable nuclei, crush artifacts Lung
- Grooves and long clefts Thyroid, urothelial, ovary, lymphoma
- Polylobulation Some adenocarcinomas
- Indentations, undulations, folds Many forms of cancer

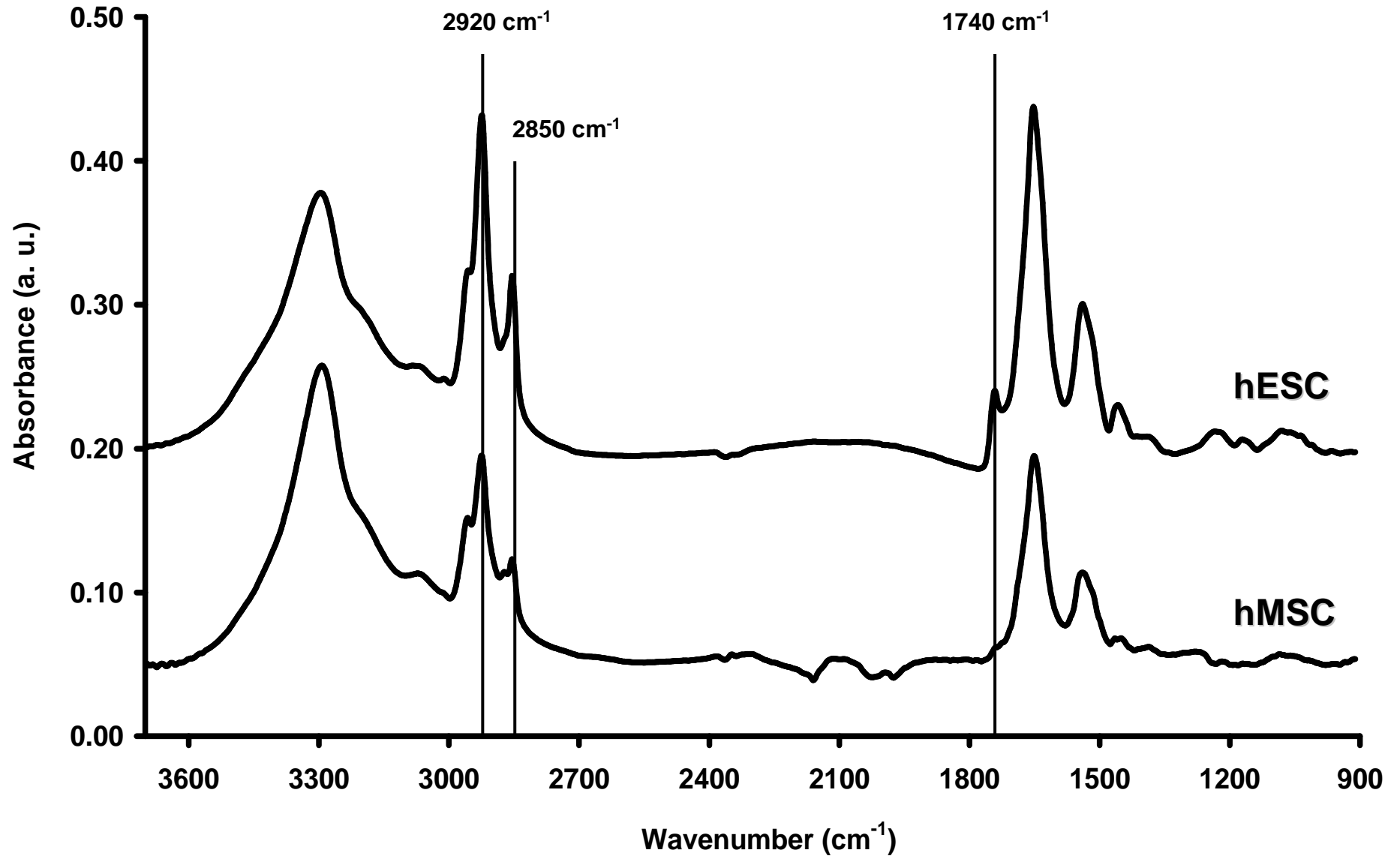
Chromatin changes

- Coarse aggregates Many forms of cancer
- Asymmetric aggregates Wide range of cancers
- Dispersed heterochromatin Lung
- Loss of aggregates Many forms of cancer

Nucleolar alterations

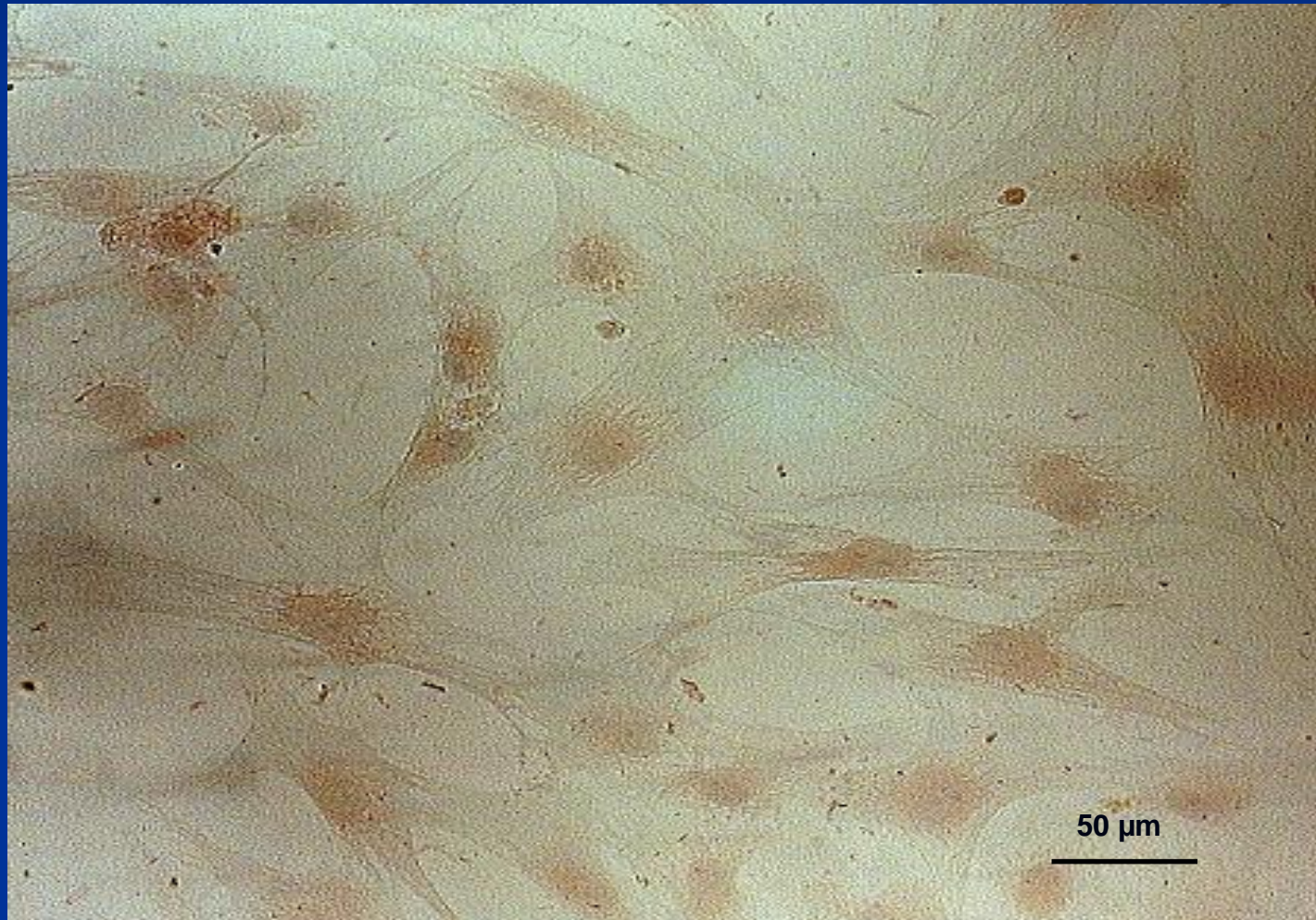
- Enlarged nucleoli Wide range of cancers
- Inconspicuous nucleoli Cervix, lung
- Variation in size Wide range of cancers

FTIR SPECTRA OF STEM CELLS

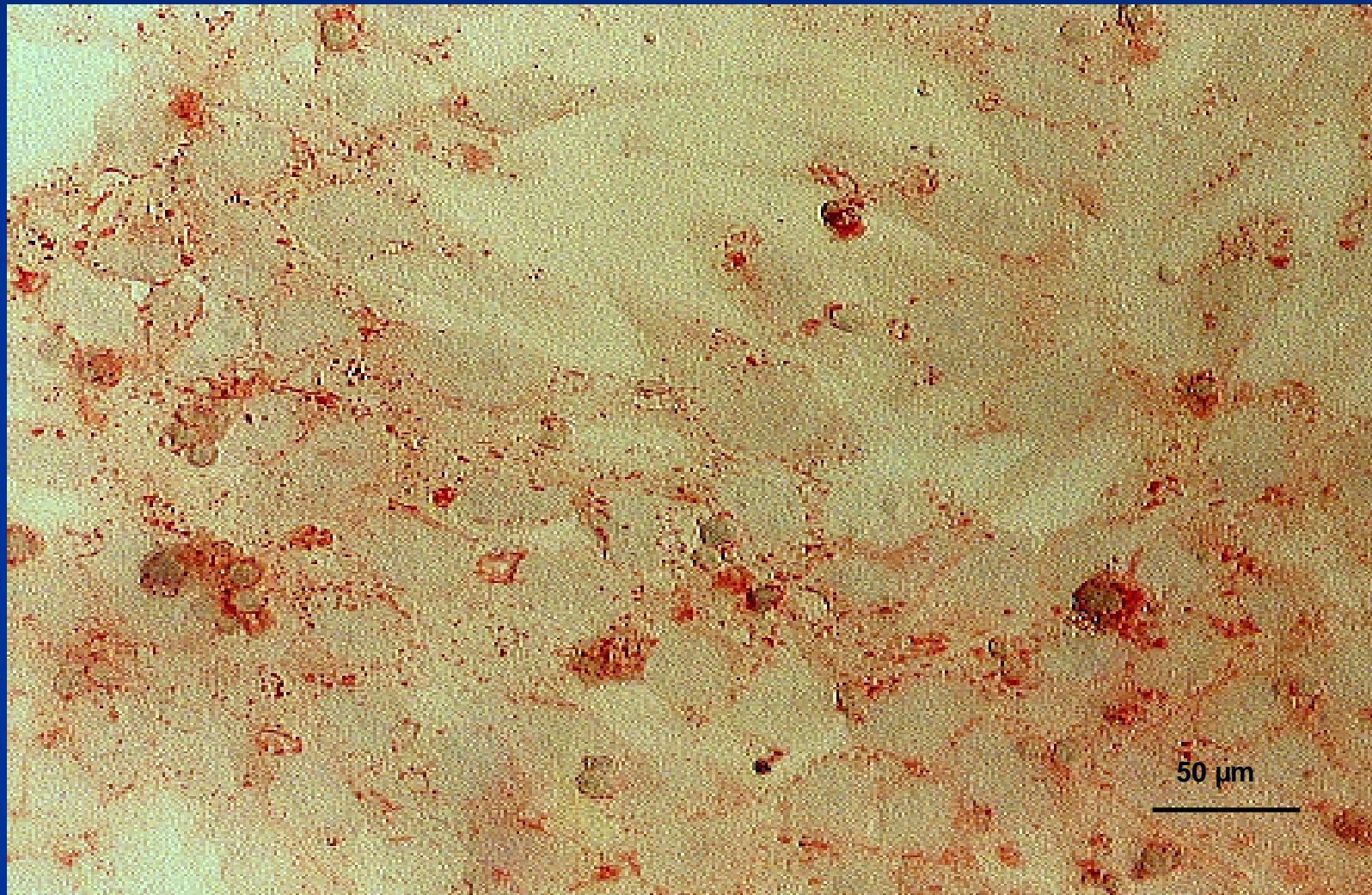


Pijanka J., *et al.* *Analyst* 135: 3126-3132; 2010.

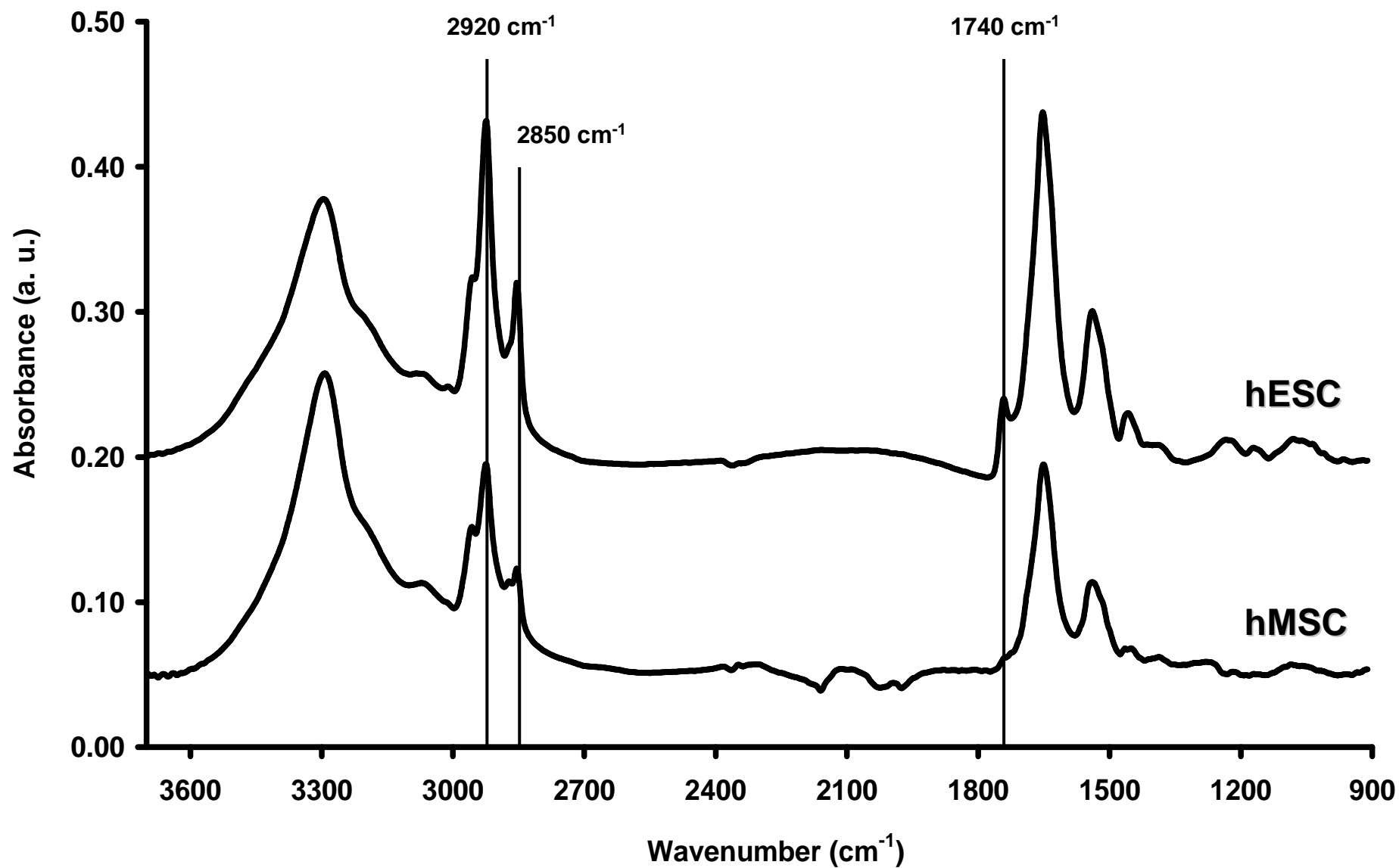
HUMAN MESENCHYMAL STEM CELLS



HUMAN EMBRYONIC STEM CELLS



FTIR SPECTRA OF STEM CELLS



Pijanka J., *et al.* *Analyst* 135: 3126-3132; 2010.

FTIR SPECTROSCOPY AND CANCER DIAGNOSIS

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QUESTION

**Can FTIR spectroscopy help in the
diagnosis
and management of cancer?**

ANSWER

Yes, but

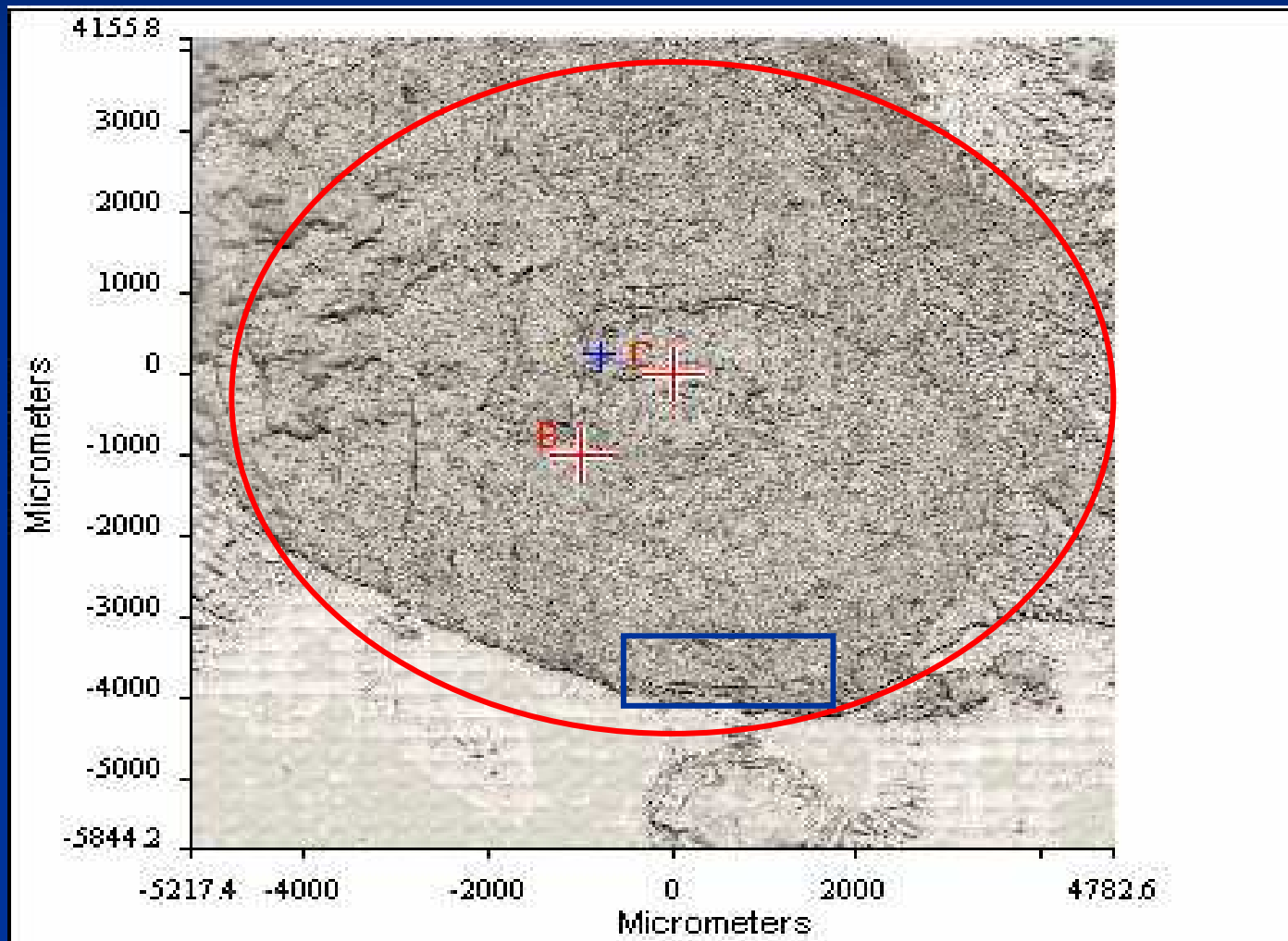
For tissue analysis, a spectroscopic model must satisfy three major criteria:

- 1. It must reproduce the essential features of the image pertinent to conventional histology.**

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- 2. Implementation must be computationally efficient to be clinically applicable.**

LYMPH NODE BIOPSY



For tissue analysis, a spectroscopic model must satisfy three major criteria:

1. It must reproduce the essential features of the image pertinent to conventional histology.
2. Implementation must be computationally efficient to be clinically applicable.
3. The model must be robust and validated in extensive studies (50 cases for pilot studies).

Bhargava R., et al., Biochim Biophys Acta. 2006.

CANCER DIAGNOSIS WITH FTIR SPECTROSCOPY

		No of patients
Yano K.	Anal Biochem, 2000	24
Salman A.	Cell Mol biol 2001	10
Argov S.	J Biomed Optics, 2002.	24
Malins D. C.	PNAS, 2003	49
Mordechai S.	J Microsc, 2003	10
Ramesh J.	J Lab Clin Med, 2003.	3
Steiner G.	Biopolymers, 2003	24
Wang J.-S.	World J Gastroenterol, 2003	27
Wood B. R.	Gynecol Oncol, 2004	10
German M.	Biophys J, 2006	6
Andrus P. G.	Technol Cancer Res treat, 2006	9
Gazi E.	Eur Urol, 2006	36
Paluszkiewicz C.	Vibrat Spectrosc, 2007	5

CONCLUSION

- **Better interaction Spectroscopists-clinicians**
- **Standardisation**
 - **Sample preparation**
 - **Data collection**
 - **Data analysis**
- **Validation**
- **Big studies (multicentre), big number of patients (statistical input)**
- **Publish in medical journals.**

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