



# Treating today's patients with tomorrow's solutions

1st conference supported by:

European Multidisciplinary Breast Cancer Collaborative (EMBCC)

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# EMBCC board members



**Dr Anne Vincent Salomon** Breast pathologist, Institut Curie, Paris

Anne Vincent-Salomon is head of the pathology department and has been practicing at the Institut Curie for 21 years. She has an MD degree from the University Paris VI and a PhD from Paris Sud University. Her domains of expertise are breast pathology, surgical pathology and haematopathology. Her deep commitment to breast pathology strongly motivated her will to reinforce the breast tumour characterisation using immunohistochemistry as well as molecular tools.

From 2003 to 2013, she received a grant twice in a row from INSERM (INTERFACE) that enabled her to gain her PhD thesis in Dr Delattre's laboratory (INSERM U830). One of the first achievements in her scientific career was identifying and validating a DNA-based prognostic signature for early small luminal HER2-neg breast carcinoma patients (Gravier *et al.*, 2010; Vincent-Salomon *et al.*, 2013). Next she pursued and extended her main domain of research interest in breast carcinoma genomics with a special focus on the heterogeneity of basal-like breast carcinomas and ductal carcinomas in situ.

In an ITMO / AVIESAN programme headed by Emmanuel Barillot, she is involved in a research program on the in situ / invasive transition in breast carcinomas. In January 2014, she joined U934 INSERM (Pr E. Heard) where she is developing projects for analysing the molecular and phenotypic heterogeneity of breast carcinomas as well as collaborative studies with different members of Pr. E. Heard's team on X chromosome re-activation in breast carcinomas (Chaligné *et al.* Genome Biology, in press).



**Dr Catherine Bouteille** Breast Surgeon, Clinique Mutualiste, Saint Etienne

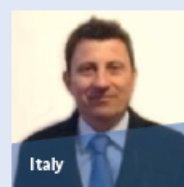
After working as a breast surgeon in the University Hospital of Saint Etienne and in the cancer centre Léon Bérard in Lyon, Dr Catherine Bouteille is now working at the Clinique Mutualiste Chirurgicale de la Loire in Saint Etienne. She manages 200 breast cancer patients per year and the clinic covers a total of 400 new cases per year.

Since 1997, she has also specialised in breast cancer surgery and breast reconstruction. She has been performing sentinel lymph node biopsy since 2002 and using molecular sentinel node analysis since 2007. She has been a member of the French Senology Society since 2000 and the French Gynaecology Society since 1993.



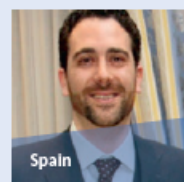
**Dr Florence Godey** Biologist, Centre Eugène Marquis, Rennes

Florence Godey is a medical biologist at the Cancer Centre in Rennes 'Centre Eugène Marquis'. She is also involved in breast cancer sentinel lymph node analysis and with the breast tumour biobank. She is a member of the Université de Rennes 1 Inserm U1085 – IRSET Team 'Death Receptor and Tumor Escape' (dir. Dr Inserm Patrick Legembre).



**Dr Andrea Gianatti** Director of Pathology Department, A. O Papa Giovanni XXIII, Bergamo

Dr Gianatti gained his degree in medicine in 1990 and specialised in pathology in 1994 at University of Pavia where he has been a fellow in the Department of Pathology until 1992. From 1992 he has been working at the Hospital Papa Giovanni XXIII of Bergamo where he was Director of the Anatomic Pathology Unit from 2010 and Director of the Department of Laboratory Medicine from 2012.



**Dr Vicente Peg Càmara** Pathologist, Vall d'Hebron University Hospital, Barcelona

Dr Vicente Peg Càmara graduated in medicine from the University of Zaragoza (Spain) in 2003 and received pathology residency training at Vall d'Hebron University Hospital (Barcelona, Spain) in 2008, in addition to an observership at the Massachusetts General Hospital in Boston (USA). He then returned to the Department of Pathology at Vall d'Hebron University Hospital, joining the Staff Attending and becoming the group leader for breast pathology. He has since led several research projects related to breast cancer and has participated in several national and international clinical trials. He is the author of numerous publications and frequent participant and speaker in scientific meetings.

His main research focuses on cell signalling pathways in breast cancer and their relationship to neoadjuvant chemotherapy treatment, as well as hypoxia states and the study of breast sentinel lymph node. He has been an Associate Professor at the Universitat Autònoma of Barcelona since 2012.



**Miss Tracey Irvine** Breast Surgeon, Royal Surrey County Hospital, Guildford

Tracey studied at Queens' College Cambridge and then did her clinical training at Guys and St Thomas' Hospital, London. She obtained the prestigious National Oncoplastic Fellowship and spent a year in Manchester working with breast and plastic surgeons learning the latest oncoplastic techniques. After a period as the Senior Registrar in Guildford she joined the consultant team in 2009. She leads the team in regular service improvement meetings and was appointed Clinical Director of the Breast Unit in 2012. Her specialist interests are implant reconstruction, risk reduction surgery, oncoplastic breast conservation and revision reconstruction. She continues the research into the management of the axilla which was started in Guildford by her senior colleagues.

## When is N staging important?

- Adapting adjuvant treatment to N staging  
Dr Fanny Le Du – Centre Eugène Marquis – Rennes
- When is N staging important? A surgeons opinion  
Dr Manuela Roncella – Ospedale Santa Chiara – Pisa
- pN status after Z0011  
Dr Vicente Peg – Hospital Universitari Vall d’Hebron - Barcelona

# When is N staging important? - Synopsis



## Controversies:

- Is axillary status (pN) still necessary? And when?

## Discussion:

- Is axillary staging still useful from a clinical point of view?
- How can pathologists provide this information when only SLN(s) is/are analyzed?

## Conclusions:



N staging is still a prognostic factor and serves for chemotherapy recommendation. Gene expression profile could overshadow it in a near future.



Even if ALND is no longer recommended after a positive SLNB, there is a need to identify patients who benefit for more aggressive locoregional treatment.



TTL classifies patients in high or low risk of recurrence and could be helpful in those cases when ALND is not performed after a positive SLNB.

## Axillary staging in DCIS

- Impact of OSNA® in patients with DCIS  
Dr Luca Di Tommaso – Istituto Clinico Humanitas Rozzano – Milan
- Axillary staging in DCIS: indications and controversies in 2016  
Dr Charlotte Ngô – Hôpital Européen Georges Pompidou– Paris

# Axillary staging in DCIS- Synopsis

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## Controversies:

- SLN biopsy and OSNA analysis in DCIS - what to do?

## Discussion:

- When is SLNB recommended in DCIS?
- Can OSNA be used for SLN analysis in DCIS?

## Conclusions:



SLNB should be performed in DCIS when suspicion of misdiagnosis, total mastectomy, and large imaging mass.



OSNA can safely be used for DCIS and should not lead to unnecessary ALND.



Positive OSNA results might lead to extensive pathological examination to detect occult invasive carcinoma.

## Axillary staging in neoadjuvant setting

- Surgical decision in case of neoadjuvant setting  
Prof Roman Rouzier – Institut Curie – Paris
- Do you copy me?? Nodal status after chemotherapy  
Dr Mark Kissin – Royal Surrey County Hospital – Guildford
- CK19 expression in breast cancer tumours after neoadjuvant chemotherapy  
Dr Begoña Vieites - Hospital Universitario Virgen del Rocío – Sevilla
- New approach to sentinel node detection in neoadjuvant setting: IMAGINE II  
Dr Antonio Piñero-Madrona - HCU "Virgen de la Arrixaca" - Murcia

# Axillary staging in neoadjuvant setting - Synopsis



## Controversies:

- Is SLNB reliable after NACT?

## Discussion:

- How can SLNB after NACT be performed best in order to increase success rates?
- Is SLNB a reliable basis for decision making? Do we over-/ undertreat?

## Conclusions:



To improve the FN rate of SLNB after NACT, dual tracer and excision of  $\geq 2$  nodes recommended. Furthermore, new detection methods (Sentimag<sup>®</sup>) can be a solution (under investigation in IMAGINE II study).



We may need to reconsider definition of SLN; use of clips can be helpful to identify SLNs .



OSNA could be used after NACT as CK19 expression is preserved and could serve as target to evaluate presence of metastases in SLNs.



## New challenge for radiotherapy

- Novel irradiation procedures in Breast Cancer  
Dr José Luis Lopez – Hospital Universitario Virgen del Rocío – Sevilla
- Surgical axillary management in case of positive sentinel lymph node  
Dr Catherine Bouteille – Clinique Mutualiste – St. Etienne
- Dilemma for the Radiation Oncologist and the importance of the OPTIMAL study  
Dr Manel Algara – Parc de Salut Mar – Barcelona

# New challenge for radiotherapy - Synopsis



## Controversies:

- What are the indications for irradiation of lymph nodes?

## Discussion:

- Can irradiation replace axillary clearance ?
- Can OSNA be used to decide which patient can benefit of irradiation?

## Conclusions:



Lymphatic areas should be irradiated for patient with  $\geq 4$  metastatic nodes.



For patients with 2 or more metastatic SNs, ALND remains the standard. Recent trials (e.g. AMAROS) suggest that it could be replaced by irradiation.



OSNA and OPTIMAL study might answer the question of irradiation for patient with low tumor burden.

- A picture from the US  
Dr Tracey Irvine – Royal Surrey County Hospital – Guildford

## A picture from the US - Synopsis

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### Controversies:

- Z0011 has been practice changing – although it has some issues

### Discussion:

- Is the US practice the same as our European practice?
- What are the US NCCN Guidelines?

### Conclusions:



Not all US units US the axilla – many still go on clinical stage.



Many units will give comprehensive radiotherapy if 1-3 nodes positive. This includes the axilla, IMC, SCF.



Extra capsular extension predicts high NSLN positivity – can we get this data from TTL or the ‘scraps’

## Is Lobular Cancer different?

- OSNA<sup>®</sup> evaluation of axillary nodes for invasive Lobular Breast Cancer  
Dr Peter Barry – Royal Marsden Hospital – London
- Lobular carcinoma's pathological and molecular specificities: new insights  
Dr Anne Vincent-Salomon – Institut Curie – Paris
- Metastatic patterns of invasive lobular carcinoma of the breast  
Dr David Hardisson – Hospital Universitario La Paz – Madrid

# Is Lobular Cancer different? - Synopsis



## Controversies:

- What are the specific characteristics of LBC?

## Discussion:

- What are the consequences of this difference ?
- Can OSNA be used in lobular carcinomas?

## Conclusions:



LBC have histological, genetic, molecular specificities (ER+, low proliferation factor, E-cadherin inactivation, ...) compared to DBC.



Although SN positivity rate is lower, LBC tends to metastasise in more LNs but without clear impact on overall survival (specific mutation patterns seems to have prognostic impact).



TTL and OSNA can be helpful as SLN histological examination in LBC is challenging.

## Axillary staging in the era of gene profiling

- Gene Profiling in Early Breast Cancer  
Dr Aleix Prat – Hospital Clínic de Barcelona – Barcelona
- Molecular profiling of primary tumor: which role in lymph node status?  
Prof Anna Sapino – IRCCS – Candiolo
- Molecular profile and sentinel Total Tumoral Load  
Dr Laia Bernet– Hospital Lluís Alcanyís – Xàtiva
- Immunohistochemistry: the link between genetic profiling and the management of breast cancer  
Dr Andrea Gianatti - Ospedale Papa Giovanni XXIII - Bergamo

# Axillary staging in the era of gene profiling - Synopsis



## Controversies:

- Is there enough evidence to show the benefit of routine use of gene profiling?

## Discussion:

- Which molecular signature for which patient?
- Combination of molecular signature and N staging?

## Conclusions:



Differences between the molecular subtype of primary tumour and N staging influence prognosis.



Only ER, PR, HER2 and Ki67 are sufficient to classify the molecular subtypes in BC at the moment.



Differences in the TTL cut-off were observed among the different molecular profiles. It could be interesting to consider a lower TTL cut-off for the more aggressive breast cancer subtypes.