Author's response to reviews

Title: Breast cancer management guidelines: does compliance depend on the local cancer organisation?

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Author's response to reviews: see over
Title: Breast cancer management guidelines: does compliance depend on the local cancer organisation?

Reponses to the reviewers

Reviewer: Antonio Ponti

1. Major compulsory revisions.

1.1. The definition of clinical practices criteria (Appendix 1 and p.5) (1). It is mentioned that criteria derive from National Clinical Guidelines but these are not referenced. Please provide a reference.

Response
Thank you for pointing out this omission. We have now added this item in an additional table listing relevant clinical practices guidelines.

1.2. The definition of clinical practice criteria (Appendix 1 and p.5) (2). The process of classifying each criterion in three levels of compliance should be clarified: in addition to those listed as Authors (who don’t include radiologists or pathologists) who are the experts and which disciplines represent (it seems their names are in the acknowledgments, it could be sufficient to explain and add the description of the discipline)? Did you attempt to reach a consensus on the final list and the description of criteria by the entire expert group or each expert was responsible solely for his/her discipline?

Response
Thank you for this pertinent comment. We have now added each discipline in the acknowledgments.

Indeed, we reached a consensus on the description of criteria by emailing the entire expert group, with particular attention to the definition of justifiable category. We have now added this point in the method section, at the end of the evaluation of compliance with practice guidelines section.

Page 6: Finally, the entire expert group reached a consensus on the description of criteria with particular attention to the justifiable category.

1.3. The definition of clinical practice criteria (Appendix 1 and p.5) (3). The classification in the three classes is rather complex and at times it seems ambiguous. Please improve punctuation or layout of the Table in order to remove the current ambiguity of interpretation (see for example criteria 1 "AND mastectomy OR conservative surgery" etc).

Response
We have modified the wording in the appendix to improve the clarity of our classification.

1.4. The definition of clinical practice criteria (Appendix 1 and p.5) (4). Management of missing values should be clarified. The way they are managed in the classification of compliance is at times contradictory: for example for criterion 3 missing values are ignored (are there any? Table 2 does not help in answering this question), for criterion 4 they are included in the J category and for criterion 5 they are included in the NC category. Although I understand this cannot be changed now, a quantification of missing
values for each variable (Table 2, at present there is one column which includes both "missing" and "not eligible") is required.

**Response**

We have added a column to the appendix to explain more precisely each criterion listed in "justifiable". Moreover, for each criterion except criterion 5, missing values were included in ‘justifiable’. We also added a quantification if there were missing values in the appendix for each criterion.

1.5. Study population (1). Can you explain briefly how informed consent was obtained and how you interpret a rather high proportion of refusers (about one third, in a study requiring data abstraction only). Was the proportion of refusers very different from Hospital to Hospital.

**Response**

We have added information regarding informed consent in the method.

Page 5: **All oncologists in both regions reported every patient with a first diagnosis of invasive non-metastatic breast cancer.** Following this, an mail explaining the aims of the study was sent to each patient, together with a consent form and a questionnaire collecting personal information. Once the consent form had been received, medical data was collected from the patient’s medical record. The logistics of data collection were carried out by a experienced research team specifically dedicated to the project, (research assistants and research practitioners).

We received 193 refusals (13%) and 269 non-responses (18%) which is due to the modality of collection since the patients were asked to answer self-administered questionnaires (satisfaction and quality of life). Moreover, the refusal seems not to be attributed to a single hospital since the management of each patient was multidisciplinary and multi-institution (made by different hospitals). This is why we didn’t provide results hospital by hospital. We add a sentence regarding this point in the results and discussion sections (limits).

Page 8: **Results**: other patients were refusals (193, 13%) or non-response (269, 18%).

Page 13: **Discussion**: Firstly, concerning the population, data collection and definition of non compliance, we cannot exclude a population selection bias since a proportion of women were not included (refusal or non response) and we included probably more patients from hospitals with high volumes (but regional data are available for comparison concerning all stages of cancer, metastatic and non metastatic BC).

1.6. Study population (2). Total eligible population was 1416 non-metastatic invasive breast cancer cases in 20 Hospitals in 16 months, which makes an average of about 50 cases per Hospital per year. Is this correct, and if so can you comment about this low average volume? Information on volume distribution in the 20 Hospitals would be useful in the Methods section of the paper.

**Response**

In France, at the time of the study, a large number of hospitals could manage surgeries in breast cancer care (from less than 10 surgery procedures to more than 500). We provide now an additional table to present surgery volume in both areas (data available from a database managed by the French Ministry of Health).
Additional table 1

<table>
<thead>
<tr>
<th>Breast cancer Surgery volume per year</th>
<th>Number of hospitals (%) (regional administrative data: mean of 2003 and 2004)</th>
<th>Number of patients (%) Reperes study</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 and less</td>
<td>13 (13)</td>
<td>19 (2)</td>
</tr>
<tr>
<td>11-50</td>
<td>35 (36)</td>
<td>137 (15)</td>
</tr>
<tr>
<td>51-150</td>
<td>29 (29)</td>
<td>414 (44)</td>
</tr>
<tr>
<td>151 and over</td>
<td>22 (22)</td>
<td>362 (39)</td>
</tr>
</tbody>
</table>

As a consequence, the average is not a relevant measure to summarise these data. We have completed the method section to explain this issue (in addition to previous studies that provide the same elements).

Page 5: These eligible patients were reported by public and private hospitals in the two regions (99 eligible hospitals: 13% with less than 11 BC surgeries per year and 51% with more than 50).

Moreover, we include only patients with non metastatic breast cancer with care management in these regions and consequently exclude all other breast cancer patients. We now discuss this selection bias in the discussion section.

Page 13: Firstly, concerning the population, data collection and definition of non compliance, we cannot exclude a population selection bias since a proportion of women were not included (refusal or non response) and we included probably more patients from hospitals with high volumes (but regional data are available for comparison concerning all stages of cancer, metastatic and non metastatic BC).

1.7. Univariate analysis. When you describe univariate analysis for therapeutic indications (p. 8) and for radiotherapy (p. 9) variables used in univariate analysis change completely. Please clarify text.

Response

Three analyses were independently carried out based on logistic modeling, non-compliance regarding 1) clinical decision for treatment, 2) radiotherapy (clinical decision for radiotherapy and radiotherapy procedure, 3) overall treatment sequence (clinical decision for treatment and therapeutic procedures). For each analysis, the same variables were used for univariate modeling. However, the variable selection process lead to three distinct final multivariate models. Variables selected for the multivariate models were either significant in the univariate analyses (p<0.20) or relevant clinical variables In method section, we reported the list of these variables (section ‘study variables’, second paragraph) and in result section, we reported only significant or relevant in univariate analysis (section ‘factors associated’).

Page 7, statistical analysis: “We examined factors associated with non-compliance with CPGs. Aside from the LCU, all variables were first fitted in univariate logistic regression models. Variables significant in the univariate analyses (p<0.20), as well as relevant clinical variables, were then fitted in a classical multivariate logistic model. This process was independently repeated for each outcome variable, non-compliance regarding 1) clinical decision for treatment, 2) radiotherapy, 3) overall treatment sequence.

1.8. Page 12: "Concerning the location of treatment, the region with a higher compliance rate had already implemented breast cancer CPGs (guidelines) when the
study started which may explain the intraregional differences.” What do you mean by implemented? It would be great if implementation of guidelines would provide such an amazing effect! This should be regarded as the main result in your paper. This may be true but needs validation. Could you also provide alternative explanations on this huge and consistent difference between the two Regions?

Response
Implementation involved a regional adaptation of national clinical guidelines with local and regional specialists and diffusion of these regional guidelines. Another possible explanation could be the implementation and diffusion of multidisciplinary meetings previously in one of the two regions. We have added these elements in the discussion section. Nevertheless, our study design cannot confirm the link between these implementations as the best results in terms of the guidelines compliance because other national or regional factors are present at the same time; for example, the first national cancer plan and the regional cancer plans in each area which have the same objectives as at the national level but which have different ways and priorities to obtain results. Finally the availability of cancer specialists was not the same across regions (region 1 has more inhabitants and more breast cancer specialists). Here, we have also added some elements in the discussion section.

Page 12: Concerning the region of BC treatment, a factor associated with non compliance, the region with a higher compliance rate had already implemented breast cancer CPGs (2004) by local specialist involvement in regional guidelines at the time of the study. This implementation could be explained partially by the regional differences. But some disparity for care accessibility (equipment or personnel resources) between the two regions could explain part of these differences, as reported by others. The more recent publications of factors related to the implementation of CGPs showed that patient factors, such as comorbidities or very short life expectancy, reduce the chance that guidelines are followed because they do not encourage the physician to prescribe aggressive therapy. Physician factors related to implementation could be seniority, lack of awareness and limited agreement with guidelines. Moreover, organisation factors such as limited time, work pressure and limited support from peers have been described as barriers to change.

2. Essential minor revisions.

2.1. You mention that your study domain concerns early breast cancer (p. 4) but inclusion criteria (p. 4) exclude metastatic from onset cancer only and in fact from Table 1 it is clear that also stage 2 or 3 cancers are included. Please correct or explain.

Response
We agreed with this remark and have replaced “early breast cancer” by “non-metastatic breast cancer” throughout the text.

2.2. The classification of compliance is described on a contradictory way in these two passages, both in page 5:
– (NC): non-compliance with CPGs and no justification available in the patient’s medical record.
– When no data were available in the medical record to classify the criterion as ‘NC’, it was considered potentially ‘justifiable’ (J).

Response
We deleted the sentence to avoid confusion and have added a column to the appendix to explain more precisely each criterion listed in “justifiable”.
2.3. Pages 8 and 9: check p of "teaching status", in one case quoted as $p=0.0004$ and in the other as $p=0.04$.

Response
We have corrected this error.

2.4. Page 10: "Until now, most publications have focused on therapeutic care management steps and do not provide details on compliance with treatment intervention indications". Please expand and clarify.

Response
We have expanded and clarified this sentence as below:

Page 11: To our knowledge, this is the first time that results of overall BC therapeutic care with details on procedures and clinical decision for treatment sequences have been reported in a large BC population. Indeed, most recent publications have only focused on single therapeutic care management step (surgery, radiotherapy or chemotherapy) according to BC stage and most do not provide details on overall compliance with clinical decisions.

3. Discretionary revisions.

3.1. Explanatory variables. Did you consider including Hospital?

Response
We have clarified the list of the variables in the method section.

Moreover, firstly, we now explain that the overall compliance with clinical guidelines for one patient cannot be connected to a single hospital in breast cancer care (for instance in Table 1, 39% of breast cancer patients had treatment in public and private sectors, i.e. in different hospitals), but to several practitioners, grouped in a local cancer unit (surgeon/ radiotherapist/chemotherapist and other specialists). Hospital volume was considered in previous publications (Bouche 2008, reference 12) which focused on a single hospital (surgery step). Secondly, in our perspective, we consider that compliance with the first care step can influence the others steps and consequently the complete treatment (all steps).


Page 14: Concerning organisational factors, we cannot relate overall compliance to the hospital's volume since the breast cancer care steps are often in different hospitals (surgery in one hospital and radiotherapy in another...) and these hospitals may have different volumes. It therefore seemed that the most interesting data was the LCU. However, we use hospital volume in a recent publication focused on surgery step.


Response
We focused in a recent publication on the determinants explaining the long delays for radiotherapy (Bouche G. Determinants of variability in waiting times for radiotherapy in
the treatment of breast cancer. Radiother Oncol 2010). The paper concludes that “The variability in waiting times for radiotherapy is principally a factor of the centre. It is important to pursue initiatives to improve the organization within radiotherapy centres and then to verify that these initiatives have succeeded in shortening waiting times.” We have added to the discussion to cover the elements of this article and other papers.

Page 12: But some disparity for care accessibility (equipment or personnel resources) between the two regions could explain part of these differences, as reported by others [28].

Page 13: Our results showed that compliance was lowest for radiotherapy lead time and multidisciplinary approach. Long radiotherapy lead times have already been reported in Italy [31] and in a critical review of the literature [28] and are partly due to lack of equipment or human resources.

**Reviewer: Mark Mccarthy**

1. Is the question posed by the authors well defined?
Partly – compliance of treatment with clinical guidelines is described; however, there are various studies in the literature of organisational factors, which should be introduced also at the beginning if this paper wishes to include these as determinants (as in the title).
Essential

*Response*

Your remark is correct and in response we have added references, particularly the two main publications of organizational factors as determinants of compliance with clinical guidelines (two best synthesis of the literature) in the introduction and the discussion sections.


Page 4: Background: Other studies in the literature emphasise organisational factors as determinants of compliance with CPGs
Page 11: Discussion, for instance: Indeed, most recent publications have only focused on single therapeutic care management step (surgery, radiotherapy or chemotherapy) according to BC stage and most do not provide details on overall compliance with clinical decisions. International studies [1, 3, 6, 17, 23-26] have found a higher compliance...

2. Are the methods appropriate and well described?
Partly – The abstract methods section should say where/how the data were abstracted, and the main methods section should give information on the observer reliability measures used and results. There should be description of the inclusion/exclusion from the whole-population sample (presumably from cancer registry), the levels of missing data and how this was managed (boot-strapping etc).
Essential
Response
– We take into account this remark with addition of elements in the abstract “Medical data was collected from the patient’s medical record in public and private hospitals (99 hospitals) of the regions”. 20 hospitals was an error which has been removed. Moreover in the text, we propose more details and refer the reader to other papers describing the inclusions methods of the REPERES study precisely.

Page 4-5: These eligible patients were reported by public and private hospitals in the two regions (99 eligible hospitals : 13% with less than 11 BC surgeries per year and 51% with more than 50). All oncologists in both regions reported every patient with a first diagnosis of invasive non-metastatic breast cancer. Following this, an email explaining the aims of the study was sent to each patient, together with a consent form and a questionnaire collecting personal information. Once the consent form had been received, medical data was collected from the patient’s medical record. The logistics of data collection were carried out by a experienced research team specifically dedicated to the project, (research assistants and research practitioners).Full details of the present design were published earlier [12, 13].
– We also provide now the missing data for all criteria (annex).

3. Are the data sound?
At present, the lack of information on population representativeness, data abstraction methods, and record completeness is a weakness (there’s a literature on use of secondary data in cancer studies).

Response
We have now added a minimum of information of the population and methods for data collection. We also added an additional table to present results according to the REPERES study and to regional administrative data (Breast cancer surgeries, data available from a database managed by the French Ministry of Health). We discuss this point as a limit of our study.

Page 5 : Methods: These eligible patients were reported by public and private hospitals in the two regions (99 eligible hospitals : 13% with less than 11 BC surgeries per year and 51% with more than 50). All oncologists in both regions reported every patient with a first diagnosis of invasive non-metastatic breast cancer. Following this, an email explaining the aims of the study was sent to each patient, together with a consent form and a questionnaire collecting personal information. Once the consent form had been received, medical data was collected from the patient’s medical record. The logistics of data collection were carried out by a experienced research team specifically dedicated to the project, (research assistants and research practitioners).Full details of the present design were published earlier [12, 13].
Page 13 :Discussion: Firstly, concerning the population, data collection and definition of non compliance, we cannot exclude a population selection bias since a proportion of women were not included (refusal or non response) and we included probably more patients from hospitals with high volumes (but regional data are available for comparison concerning all stages of cancer, metastatic and non metastatic BC).

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
These items are not mentioned anywhere.

Response
Of course, we omitted this important mention in our cover letter and we reviewed all text to follow the standard guidelines for cohort studies (Strobe statement).

Essential
5. Are the discussion and conclusions well balanced and adequately supported by the data?
Mostly. However, using a 'justifiable' category is challengeable, since clinical guidelines should be clear. The methods say that absent data were classified as 'justifiable', but not excluded from the study, so we don't really know the true measures. The choice to add 'justifiable' to non-compliant would seem appropriate.

Response
To answer your comment we have added a column to the appendix to explain more precisely each criterion listed in "justifiable" (definition and quantification). Moreover, to explain our choice (clarity of guidelines recommendations) we added elements in the discussion section.

Page 13:... our primary interest was to specifically assess determinants of non-compliance/non-conformity to CPGs, without distinguishing compliant and justifiable decisions, which we considered as equivalent. Indeed, from a practical point of view, it is best to specifically target those factors associated with non-compliance so that actions can be undertaken.

6. Are limitations of the work clearly stated?
These authors don't describe any limitations as such, nor more modern approaches to structured writing of the discussion section.

Response
In response we have defined the limits of our study in the discussion which is now restructured according STROBE statement (www.strobe-statement.org/). For instance, to begin the discussion

Page 11: This study showed three main results: BC compliance, factors associated with non-compliance and a multidisciplinary and multi-hospital organisation to BC care which explains the variability in BC practices. Together these results can be used to enhance BC care.

And page 13: This study has a number of strengths and limitations

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Well, there is a fair sprinkling of literature on clinical guideline comparisons, but I wonder if they searched for a more formal overview. I am not sure what the second sentence of the discussion refers to. 'To our knowledge, this is this first time that results of such investigations have been reported.' I think the first published paper comparing breast cancer treatment practice with guidelines from data in the 1980s was by McCarthy & Bore (European Journal of Cancer and Clinical Oncology 1991, 27, 579-582), and there were several subsequently. The authors could track this literature, and also the literature on organisational factors in cancer care.

Response
We confirm that we have tracked the literature of these topics (compliance with breast cancer care and organizational factor in cancer care) even if we omitted to mention the main papers. We have now added main papers in the introduction and discussion sections.

Background, page 4: Other studies in the literature emphasise organisational factors as determinants of compliance with CPGs [6-11].
Finally, we have reformulated our sentence to best reflect our idea.
Page 11: To our knowledge, this is the first time that results of overall BC therapeutic care with details on procedures and clinical decision for treatment sequences have been reported in a large BC population. Indeed, most recent publications have only focused on single therapeutic care management step (surgery, radiotherapy or chemotherapy) according to BC stage and most do not provide details on overall compliance with clinical decisions.

8. Do the title and abstract accurately convey what has been found?
No. The abstract results should describe local cancer organisation (not just practice) for the title and abstract conclusion to be justified.

But as there is little in the main paper about organisation (only private/public hospital, region and teaching status, data are taken from medical records), the second objective set at the beginning of the paper 'to identify factors associated with non-compliance at a clinical and organisational level (LCU)' is difficult to demonstrate ('Finally, introducing the LCU as a random effect significantly decreased the residual variability (LRT, p<0.05), suggesting the presence of heterogeneity of compliance in overall treatment sequence across LCUs and reinforcing the need to keep this variable in our model.')

The final 'positive' regression results should not attributed to patients being non-compliant, but surely to the doctors!

Essential

Response
We added another sentence to the end of the results section of the abstract, summarizing how we observed heterogeneity of practice between cancer units.

Abstract, page 3: Finally, heterogeneity of compliance in overall treatment sequence was identified between local cancer unit (p<0.05)

We also added other remarks from available data on organizational determinants (a limit in the new discussion section) as the interpretation of LCU result (heterogeneity across LCU). But the management of breast cancer is multidisciplinary, and in France, often multihospital (for instance public and private). It therefore seemed that the most interesting data to capture different organizational factors and to propose actions was the LCU.

Discussion, Page 13: Another potential limitation of our results was the availability of data in medical records to explain non compliance and our choice of professionals or organisational factors. We could not collect all data on every professional (for instance, experience or age) but BC management is multidisciplinary and several specialists are involved in medical decisions at each BC management step. ....

Discussion, Page 15: Currently, the implementation of the regional guidelines cannot be used as the only factor to explain a better compliance in one region. Indeed, it is well known that adherence with these guidelines depends on many other factors such as guideline, professionals', patients' and environmental characteristics.

9. Is the writing acceptable?
There could be more lively writing of the discussion, which is rather opaque at present (eg see quotation above).
Discretionary

Response
All sections were modified to take into account this remark
Reviewer: Erin Strumpf

• Major Compulsory Revisions

1. Explanatory variables include patient-, tumor-, and healthcare-system level variables. You could be more explicit about the “literature review” that these come from. From literatures on practice variations and organizational behavior, I would also expect physician- and institution-level characteristics (beyond teaching status) to be important predictors of practice and treatment patterns, and therefore compliance with CPGs. Since you have detailed clinical records, can you not extract provider or institution IDs, if not actual characteristics? Being able to include such variables, compare their importance with the ones you currently include and/or examining their marginal contribution after controlling for other factors seems like it would be a significant contribution.

Response
We added two main publications of organizational factors as determinants of compliance with clinical guidelines (particularly, the two best syntheses of the literature) in the introduction and the discussion sections. The care management of breast cancer is multidisciplinary, and in France, often multihospital (for instance public and private; Cf Table 1 39% in our study). It therefore seemed that the most interesting data to capture different organizational factors and to propose actions was the LCU. Today, institutional factors were limited to procedure volume; the medical record could provide the medical provider but you explain now that this information was not relevant while the multidisciplinary meeting and organization in local cancer unit seems more relevant. The major difference between LCUs was the number of specialists, particularly in the big institutions, that were also the teaching institution. We added these elements in discussion section.

Discussion, Page 14: Another potential limitation of our results was the availability of data in medical records to explain non compliance and our choice of professionals or organisational factors. We could not collect all data on every professional (for instance, experience or age) but BC management is multidisciplinary and several specialists are involved in medical decisions at each BC management step. Concerning organisational factors, we cannot relate overall compliance to the hospital’s volume since the breast cancer care steps are often in different hospitals (surgery in one hospital and radiotherapy in another...) and these hospitals may have different volumes. It therefore seemed that the most interesting data was the LCU. However, we use hospital volume in a recent publication focused on surgery step.

2. You also have a very interesting context in which to explore whether, and how, different providers and institutions treat “similar” patients differently. This would tie into literatures on disparities in cancer treatment and outcomes across SES groups and on provider discrimination. How much of the variation in treatment patterns/compliance with CPGs is coming from variation within vs across providers?

Response
We only have few available data on SES status in medical records (age; educational level, family status) and we chose to explore these variables firstly in this paper. But in a recent publication limited to radiotherapy we showed that SES variables did not explain radiotherapy delays (reference 33 in this revision). We chose for a future study to explore more SES variables through the possible availability of these data in France. This point is probably a limit in our study.

3. In the results for factors associated with treatment compliance, you cite patient age, hospital status and region as maintaining significant associations in the multivariate and
mixed models. The implications of these results require more discussion: does this reflect patient preferences? The appropriateness of treatments? Does this infer that the CPGs are “wrong” in certain cases? It seems to me that your criteria of NC vs J actually gives you quite a bit of information to address these questions that you are essentially throwing away by only considering a binary outcome. I would suggest using 3 outcome categories and a multinomial logistic regression model in order to understand how your right-hand side variables are predicting each of the 3 outcomes, since the distinction between C and J is actually meaningful.

Response
We have discussed the implications of these results in greater detail in this modified paper.

For instance, page 12: But some disparity for care accessibility (equipment or personnel resources) between the two regions could explain part of these differences, as reported by others [28]. The more recent publications of factors related to the implementation of CPGs showed that patient factors, such as comorbidities or very short life expectancy, reduce the chance that guidelines are followed because they do not encourage the physician to prescribe aggressive therapy. Physician factors related to implementation could be seniority, lack of awareness and limited agreement with guidelines. Moreover, organisation factors such as limited time, work pressure and limited support from peers have been described as barriers to change.

For the point related to the statistical approach: Polychotomous regression is appropriate when the outcome variable is nominal with more than two levels. In our study, a medical decision could be non compliant to CPG’s, compliant or justifiable. However, our primary interest was to specifically assess determinants of non compliance / non conformity to CPG, without distinguishing compliant and justifiable decisions, which we considered equivalent. Indeed, from a practical view, it is best to specifically target those factors associated with non compliance so that actions can be undertaken. In view of these objectives, logistic regression using two levels was the most optimal modeling approach. We have now included this comment into the discussion section.

Page 14: Another statistical choice could be an analysis with three levels of compliance (a polychotomous regression). However, our primary interest was to specifically assess determinants of non compliance/non conformity to CPGs, without distinguishing compliant and justifiable decisions, which we considered as equivalent. Indeed, from a practical point of view, it is best to specifically target those factors associated with non compliance so that actions can be undertaken. In view of these objectives, logistic regression using two levels was the optimal modelling approach.

4. Your discussion section, as it currently stands, gives the reader no sense that this research contributes to the literature beyond what has already been done. You need to do a better job of clarifying your contribution with this study.

Response
We followed the STROBE statement on reporting of cohort studies to construct this article and we improve the discussion section.

Page 11: This study showed three main results: BC compliance, factors associated with non-compliance and a multidisciplinary and multi-hospital organisation to BC care which explains the variability in BC practices. Together these results can be used to enhance BC care.
And page 13: This study has a number of strengths and limitations

5. In the beginning of the discussion, you acknowledge the importance of delay to radiotherapy in driving your results. What are important system-level factors that would
affect these delays? Have there been changes to them? Can you explore this in your empirical analysis? I saw this as a major gap that you did not address.

**Response**

We now added references to discuss the delay of radiotherapy. Discussion, page 13: *Our results showed that compliance was lowest for radiotherapy lead time and multidisciplinary approach. Long radiotherapy lead times have already been reported in France [28] and Italy [31] and are partly due to lack of equipment or human resources.*

Moreover, we published a special study of breast cancer radiotherapy: Bouche G, Ingrand I, Mathoulin-Péllissier S, Ingrand P, Breton-Callu C, Migeot V. **Determinants of variability in waiting times for radiotherapy in the treatment of breast cancer.** Radiother Oncol 2010 (reference 33).

6. You motivate the paper in part by describing recent policies to create LCUs and implement CPGs. However, it is unclear where your data fall with respect to the implementation timing of these policies. It would be helpful to clarify this. Further, in the discussion you acknowledge that one of your two regions had already implemented breast cancer CPGs before your study period. It seems to me that you have the potential to answer some very interesting and relevant questions (for both health policy and public health) in terms of the impact of such policies, though it's not clear you can do so with the data presented here.

**Response**

LCUs were implemented in 2003 and the regional breast cancer CPGs were implemented at the same times with diffusion in 2004 (the last update in national guidelines has been available since 2002). Our eligible patients were selected from June 2003 to October 2004.

We verified that these elements are provided in the text and added an additional table to list the BC guidelines during the same period.

**Discussion section, page 12:** *Concerning the region of BC treatment, a factor associated with non compliance, the region with a higher compliance rate had already implemented breast cancer CPGs (2004) by local specialist involvement in regional guidelines at the time of the study.*

**Additional table 2:** National and international Clinical Practice Guidelines for the management of non metastatic breast cancer published before 2004

<table>
<thead>
<tr>
<th>Year</th>
<th>CPG</th>
<th>Society</th>
<th>Internet link</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>Chirurgie des lésions mammaires : prise en charge de première intention</td>
<td>Agence Nationale d'Accréditation et d'Évaluation en Santé (ANAES)</td>
<td><a href="http://www.has-sante.fr/">http://www.has-sante.fr/</a></td>
</tr>
<tr>
<td>Country</td>
<td>Year</td>
<td>Title</td>
<td>Organization</td>
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<tr>
<td></td>
<td>1998</td>
<td>Guidelines for surgeons in the management of symptomatic breast disease in the united kingdom</td>
<td>British Association of Surgical Oncology (BASO) - Association of Breast Surgery (ABS)</td>
</tr>
</tbody>
</table>

7. More emphasis on explaining how this work relates to public health, rather than health services research, is needed for this particular journal.

*Response*

We think that in this study the breast cancer subject, the methodology and the data (not the administrative files but medical records) as the context of analysis (compliance to clinical guidelines with an expert physician consensus) are relevant for colleagues reading BMC public health.