ANNEX I

MODIFICATIONS INTRODUCED IN THE DOCTORAL THESIS AFTER CONSIDERATION OF THE EXTERNAL EXPERTS REVIEW

THESIS TITLE:

Software solutions for two computationally intensive problems: reconstruction of dynamic MRI and handling of alpha-stable distributions

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ADVISORS:

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1 Forewords

I would like to thank the external experts the careful revision of the thesis and their valuable comments, specially those pointing out the main weaknesses of the work and their recommendations to improve the global result.

Since the current Thesis is presented as a compendium of publications, no changes can be introduced in the main chapters of the document (Chapters 2 to 8). Nevertheless, an effort has been made to satisfy the reviewers requirements by improving the introduction, methodology, discussion and limitation sections of the Thesis.

The main changes involve the inclusion of a background section in the introduction chapter in which a the main aspects and related methods dealing with Magnetic Resonance Imaging reconstruction and alpha-stable distributions are reviewed.

I consider that the general quality of the Thesis has been positively affected by the reviewers recommendations.

2 First assessment report

ASSESSMENT REPORT OF A PhD THESIS PRIOR TO ITS DEFENSE

(As required by Section 2.1c. of the Regulation concerning doctoral thesis defense at UVa)

Full name:...**Justin Haldar**.....

Department: ...**Ming Hsieh Department of Electrical Engineering**.....

University or Research Institution: ...**University of Southern California**.....

Regarding the thesis entitled:.....**Software solutions for two computationally intensive problems: Reconstruction of dynamic MR and handling of alpha-stable distributions**...

Written by Mr./Mrs.: ...**D. Javier Royuela del Val**.....

Please, report your arguments and critical opinion on the following issues concerning the PhD thesis, writing as much as necessary:

1. Is the topic relevant? Are the research objectives well defined?

   Accelerated cardiac MRI is an important problem that many groups are pursuing. The relevance of this work is underscored by the fact that several chapters have been published in some of the top journals and conferences in the field. The research objectives are well defined and clearly outlined.

2. Is the selected methodology sound and suitable for the topic and the objectives pursued in the thesis?

   The problem formulations are sound and suitable for the topic and the objectives pursued in this work.

   The thesis does not discuss convergence properties of the proposed algorithm. It is likely that the algorithm will converge to suboptimal local minima unless initialized well.

   The thesis does not discuss the limitations of simulating data acquisition based on DICOM images. One of the major problems with this approach is that the image loses its phase information, which increases the amount of redundancy that's present in k-space (symmetry properties of the Fourier transform). This may lead to better performance with DICOM images than could be achieved with real data. Similarly, the XCAT phantom is extremely sparse relative to real MRI data, and is both real-valued (no phase) and piecewise constant (which makes TV an ideal constraint). This may also artificially improve the performance of the proposed approach. These issues are hard to avoid, though caveats should be clearly described since the use of these simulation objects may lead to some bias in the results.

3. Is the body of reviewed literature up to date and complete? Have all relevant sources been considered and cited?

   The literature review on dynamic cardiac MRI is not very complete and not very up-to-date. The paper does not discuss some of the important contributions and innovations from many of the world's top accelerated cardiac imaging groups, including: Leslie Ying's group, Zhi-Pei Liang's group, Mathews Jacob's group, Josh Trzasko's group, Reza Nezafat's group, Miki Lustig's group, John

Pauly's group, Jo Hajnal's group, Dong Liang's group, Orlando Simonetti's group, Krishna Nayak's group, etc.

The literature review has a strong focus on sparsity, but sparsity constraints alone have been overtaken in popularity over the past several years due to toher novel models that have been proposed (e.g., various forms of low-rank modeling have become popular, often combined with sparse modeling).

The literature review on motion estimation in reconstruction is also out-of-date and incomplete. Only three MRI-based approaches are discussed (Jung and Ye, Asif et al, Cordero-Grande et al), but there are several other MRI methods that have not been mentioned. In addition, there are several methods developed for other modalities like PET and CT that have not been mentioned but have a high degree of similarity to MRI methods (e.g., by Jeff Fessler's group).

4. Does the thesis make original contributions that expand the current knowledge on the subject? Are these contributions relevant?

   The thesis makes several original contributions and expands current knowledge on the subject. These contributions are also highly relevant to the field. The author would not have been able to publish papers in good journals if this were not the case.

5. Is the thesis structure adequate to explain the research carried out and the results achieved? Is language used properly? Are formal elements, like figures or tables, well laid out and helpful to understand the research and results?

   The thesis has a very clear organization, and is very easy to follow. The figures and tables are well designed and easy to interpret. English quality is good in general, though there is some minor room for improvement.

6. Only if this is a compilation thesis (written in the format of a collection of articles): Is there a clear and coherent connection among the topics and methodology of the different articles that comprise the thesis? Do the introduction and conclusions of the thesis provide a unifying picture of the whole research?
   The two topics of this thesis (dynamic MRI reconstruction and alpha-stable distribution estimation) are very different from one another, and are hard to unify. The thesis has done a reasonable job of unifying these topics under the umbrella of computationally-intensive problems. However, there is still a disconnect between the topics because they are so different from each other. I am satisfied with the current amount of cohesiveness, because I don't have any suggestions on how to improve it. The thesis would be more cohesive if chapter 8 were removed, although that may not be desirable.

7. Please mention three strengths and three weaknesses of this thesis.

   First weakness: the literature review is not very deep or complete, which gives the impression that the author may not know very much about either the history or the current trends in dynamic MRI.

   Second weakness: The thesis relies heavily on optimization tools, but does not discuss some of the optimization challenges of the proposed formulation compared to other approaches. Specifically, the proposed cost functions are non-convex, and I imagine it would be easy to get a bad result when

starting from a bad initialization. However, several other approaches would be more resilient to this kind of problem.

Third weakness: The thesis does not acknowledge or discuss the unrealistic nature of some of the simulations that are being performed. Good science should be unbiased, describing both the strengths and weaknesses of the methods that are used. However, this thesis tends to focus only on the strengths. In addition, many of the comparisons against other methods do not rely on state-of-the-art methods. Many would disagree that K-T SPARSE SENSE and MASTeR are state-of-the-art methods compared to many of the techniques that have emerged more recently in this rapidly evolving field.

8. If you think the thesis should NOT be defended in its current form, please mention the changes that you consider MUST be done before it can proceed to defense.

   The literature review should be updated to include recent references that represent the current trends in the field, as well as to acknowledge the wide variety of techniques that have been developed since the early days of the field. The literature review is much too narrow and incomplete in its current form.

   The thesis should also be careful to point out the potential limitations of using unrealistic simulations based on DICOM images or the XCAT phantom. To avoid bias, it is important that relevant caveats are clearly stated.

9. Please mention other changes that MAY be done in order to improve the thesis quality, but that you do not consider strictly necessary to authorize its defense.

   A discussion of algorithm initialization and convergence issues would increase the depth of the thesis.

   Consider whether or not the material about alpha-stable distributions is worth including in the thesis. I think the MRI content could suffice for a doctoral degree, and the thesis would be substantially more cohesive if this additional content were removed.

10. Any other comments:

    This is strong work overall, and the author should be proud of the accomplishments he has been able to make during his doctoral studies. The thesis is in fairly good shape in its current form, although the principal concern is that the literature review is shallow and out-of-date. It is important to address this concern in order to more strongly establish the expertise of the author within his primary field of research.

11. Please provide your recommendation to the Academic Board of the PhD Program:

    ☐ This thesis should be ADMITTED for defense, either in its current form or after taking into account the suggestions made in point 9 of this report.

    ☐ This thesis should be MODIFIED before its admission for defense in order to make the changes requested in point 8 of this report.

    ☐ This thesis should be REJECTED for defense, due to the arguments given in this report.

Universidad de Valladolid

Escuela de Doctorado Universidad de Valladolid

Form 2T

Place and date: .....Los Angeles, CA, March 6, 2017.....

Signature:

Notes: The length of this report is not restricted. Please remember to sign it (digital signatures are accepted).

3 Second assessment report

ASSESSMENT REPORT OF A PhD THESIS PRIOR TO ITS DEFENSE

(As required by Section 2.1c. of the Regulation concerning doctoral thesis defense at UVa)

Full name: Javier Royuela del Val
Department: Teoría de la Señal y Comunicaciones e Ingeniería Telemática
University or Research Institution**:** Universidad de Valladolid
Regarding the thesis entitled: Software solutions for two computationally intensive problems: reconstruction of dynamic MR and handling of alpha-stable distributions
Written by Mr./Mrs.: Juan Felipe Pérez-Juste Abascal

Please, report your arguments and critical opinion on the following issues concerning the PhD thesis, writing as much as necessary:

1. Is the topic relevant? Are the research objectives well defined?
   This work covers two very important topics: image reconstruction based on the compressed sensing method for accelerated dynamic MR imaging and numerical computation of alpha-stable distributions. The first topic is among the topics that has received the widest attention in recent years and addresses important clinical and computational challenges. The second topic has also been of great interest in the last few years, given the raised interest in alpha-stable distributions for modeling impulsive data.

   Objectives for the two topics as well as more specific subobjectives are clear and describe well the problems covered in this work. For the first topic, main specific objectives are to provide a robust and efficient method to estimate heart and respiratory motion and to use this information in the reconstruction procedure in order to improve image reconstruction from high undersampled data. Another subobjective is to validate the feasibility of the proposed methods for measuring cardiac function. For the second topic, the main objectives are to provide and validate an accurate and efficient tool for alpha-stable distributions.

2. Is the selected methodology sound and suitable for the topic and the objectives pursued in the thesis?
   The proposed methodology is well suited, complete and of high standard. For the first topic, proposed algorithms are compared with the state-of-the art methods and are evaluated on data from both healthy volunteers and patients, by using quantitative and qualitative metrics. In addition, the proposed methodology is combined with an efficient nonuniform sampling technique to achieve the highest possible acceleration factor and is assessed for whole heart imaging during breath hold and during free-breathing acquisition. For the second topic the proposed methodology is validated against the state-of-the art and a new toolbox is provided and described.

3. Is the body of reviewed literature up to date and complete? Have all relevant sources been considered and cited?

   The most relevant references have been included.

4. Does the thesis make original contributions that expand the current knowledge on the subject? Are these contributions relevant?
   The contributions of the thesis are of high standard and overall the presented work is very impressive. For the first topic, the proposed motion-based reconstruction methods provide significant improvement from previous methods, in image quality, robustness and acceleration factor achieved. In addition, methods have been evaluated for correcting cardiac and respiratory motion and for whole

heart imaging during breath hold and during free-breathing acquisition, which provides an overall extensive assessment and contribution.
For the second topic, the proposed method led to high increase in performance with respect to the state of the art. In addition, an efficient toolbox with MATLAB and R front-ends is provided, which should increase the impact of this work.

5. Is the thesis structure adequate to explain the research carried out and the results achieved? Is language used properly? Are formal elements, like figures or tables, well laid out and helpful to understand the research and results?
   The thesis is well structure based on a short introduction that presents all contributions, followed by all published peer-reviewed or conference publications. Figures and videos provided as supporting material help to appreciate the improvements achieved in image quality.

6. Only if this is a compilation thesis (written in the format of a collection of articles): Is there a clear and coherent connection among the topics and methodology of the different articles that comprise the thesis? Do the introduction and conclusions of the thesis provide a unifying picture of the whole research?
   The introduction provides a full picture of the contributions as well as the connections between the different contributions. Conclusions are clear and added limitations and future work provide extra overview of the final state of the work.

7. Please mention three strengths and three weaknesses of this thesis.
   Strengths: 1) High standard work presented in the three peer-review publications and the code provided for the proposed methods, which constitutes the core of this work. 2) Extensive validation of the proposed methods on different scenarios and achieved improvements with respect to the state-of-the art. 3) The thesis as a whole provides a very complete overview of the problem (for the first topic) on different paradigms, which results in a very interesting read and manuscript as a whole.

   Weaknesses perceived are presented below but they are minor in comparison with the high quality work that constitutes this thesis. 1) Short introduction and final conclusion, but as they clearly present and summarize the contributions, larger sections may lose in clarity. 2) Unbalanced contributions between the two topics, given that the achievements for the first topic are numerous and methods are assessed on different scenarios. The second topic, however, is well covered by providing a more efficient toolbox than the current state-of-the art. 3) Unbalanced length between peer-reviewed publications and conference records, but the conference publications provides further evaluations of the proposed methods on different scenarios, which is of high interest.

8. If you think the thesis should NOT be defended in its current form, please mention the changes that you consider MUST be done before it can proceed to defense.
   I think it is a very nice work that could be presented in its current form.

9. Please mention other changes that MAY be done in order to improve the thesis quality, but that you do not consider strictly necessary to authorize its defense.
   Minor corrections and typos are provided as follows. P.2 para. 2 typo after ‘have show’. P.2 para. 2: When introducing alpha-stable distributions in the introduction give some examples of their use in couple of sentences. P.9 typo after ‘since only’. P.23 typo at ‘corresponding RE values’. P.27 typo in legend after ‘1.5T data’. P. 29 typo legend parenthesis. P.60 typo after ‘angular separation given’. P.61 typo ‘and tor’. P.80 ‘minimize’ on formula (7.1). P.102 ‘10^-8’

10. Any other comments:
    I would suggest to present this thesis for a doctoral thesis award.

11. Please provide your recommendation to the Academic Board of the PhD Program:

- ☑ This thesis should be ADMITTED for defense, either in its current form or after taking into account the suggestions made in point 9 of this report.
- ☐ This thesis should be MODIFIED before its admission for defense in order to make the changes requested in point 8 of this report.
- ☐ This thesis should be REJECTED for defense, due to the arguments given in this report.

Place and date: Villeurbanne, 31/01/2017

Signature: .....

Notes: The length of this report is not restricted. Please remember to sign it (digital signatures are accepted).

4 Major changes required and modifications introduced

In the following lines, the issues raised by the external reviewers are written in *italics*. The modifications introduced in the Thesis document to satisfy the requirements are indicated in blue color; comments are written in regular font.

1 *The literature review should be updated to include recent references that represent the current trends in the field, as well as to acknowledge the wide variety of techniques that have been developed since the early years of the field. The literature review is much too narrow and incomplete in its current form.*

In his report, the reviewer mentions a whole family of MRI reconstruction methods presented in the recent literature that cover different approaches other than pure compressed sensing based methods. The methods mentioned include low-rank based methods and partially separable model based methods.

Regarding MRI reconstruction, the main hypothesis of this Thesis is that by introducing an accurate and robust motion estimation technique during the reconstruction procedure a sparser representation of the images under reconstruction can be obtained and, therefore, either the quality of the recovered images can be improved for a predefined acceleration factor or the acceleration factor can be increased for a given quality level. Therefore, sparsity-based methods with and without motion estimation described in the literature have been used for comparison in Chapters 2 through 7 (including, needless to say, the archival publications). This way, we have been able to analyze the specific contribution of the robust motion estimation technique proposed for this application during the reconstruction.

Nevertheless, in order to improve this aspect of the Thesis two kinds of modifications have been introduced:

- **First**, the main hypothesis of the Thesis has been clarified in the introduction and objectives sections. A new motivation section has been introduced separated from the background section. Aside from other minor modifications, the following paragraphs have been significantly modified or introduced:

- Motivation section, page 3, second paragraph:

One relevant drawback of the previous methods is the negative effect of motion in the low–rankness or sparsity of the images at hand, what limits the quality of the reconstructions and the maximum achievable acceleration factor. Some methods in the literature already address this aspect by introducing some kind of knowledge about this specific motion in the reconstruction procedure (Jung et al., 2009; Asif et al., 2013; Lingala et al., 2014; Mohsin et al., 2017) and have shown that the quality of the reconstruction improves when motion is considered during reconstruction. In these cases, a more complete model of the signal generation is considered, what explains their superior performance. Since we are facing a reconstruction problem, motion has to be extracted from the images under reconstruction themselves, which, in general, will be of limited quality and will also be affected by undersampling artifacts given the accelerated acquisition.

One of the main objectives of this Thesis is to develop and provide a better model for the images under reconstruction in CS based techniques when motion is present. We hypothesize that introducing an accurate and robust motion estimation (ME) technique during reconstruction can increase the sparsity of the representation and therefore the quality of the recovered images will improve for a given acceleration factor or, alternatively, higher acceleration factors will be achieved for the same reconstruction quality.

- Objectives section, page 16 onwards:

The main objective can be divided in the following individual objectives:

1. To propose a better model for the reconstruction of dynamic MR images from highly undersampled data that takes into account not only the sparsity present in natural images, but also the time redundancy of the motion that takes place in those images, as well as to provide the software tools needed for its application. In particular,

we focus on the reconstruction of cine cardiac MR images, in which the motion of the heart along the cardiac cycle is studied.

[...]

(b) To propose and develop dynamic MRI reconstruction methods that incorporate the knowledge about the heart motion in the procedure in order to obtain a sparser representation of the images at hand and to test the hypothesis about the effect of the introduction of the motion information by comparing the results obtained with those from related methods that 1) do not consider motion at all or 2) apply different ME techniques not so robust against undersampling.

- Methodology section, page 18, first paragraph

As previously described, one the the main objectives of this Thesis is to validate the hypothesis that introducing an accurate and robust ME technique improves the results obtained in CS based reconstructions. Therefore, and throughout all the work presented in this Thesis, comparisons and validations have been done against related CS methods and the effect of the ME in the sparsity of the images analyzed.

- **Second**, an update of the literature has been carried out including those methods based on low—rank restricted reconstruction and partially separable models. In the motivation section these methods are summarized and their main aspects are introduced in the background section. These methods are considered in the conclusion section as well, both in the limitations and future work subsections:

  - Motivation section, page 3, first paragraph:

  Over the last years, a wide range of new reconstruction techniques have been developed that do not rely on new hardware developments, but in the application of advanced signal processing techniques that allow to reconstruct the images from just a fraction of the data originally needed, shortening acquisition time consequently. These methods exploit the redundancy naturally present in real images. In low–rank related methods, data are assumed to be well described by a low dimensional space —with much lower dimensions than the number of data points— (Lingala et al., 2011). This low–rank structure is strictly imposed in partially separable (PS) techniques (Liang, 2007), in which a small set of

temporal basis functions are learned from low spatial resolution data. In compressed sensing (CS) theory (Donoho, 2006), the low–dimensional structure is described by a known transform —in this discipline, the sparse domain—, in which our image can be represented with a few non zero coefficients. In dictionary learning (DL) methods (Caballero et al., 2014) the basis for the representation is learned from a set of training data.

- Background section, page 4 to 17

A whole new backgroud section is included that reviews the methods and techniques present in the literature and involved in the development of this Doctoral Thesis.

- Limitations section, page 134, first paragraphs

Throuough this Thesis the proposed methods have been compared with CS–based methods in which only sparsity is considered as a regularization term. However, low–rank and PS approaches have not been considered although they have shown promising results in recent years in different MRI applications such as T1 weighted imaging of the brain (Haldar and Zhuo, 2016) and cardiac perfusion analysis (Lingala et al., 2011). PS methods have recently provided extremely high temporal resolution images of the full vocal tract (Fu et al., 2017). Both low–rank and PS methods have been combined with sparse regularizations and successfully applied to cardiac cine (Zhao et al., 2012; Miao et al., 2016), T1 and T2 mapping (Zhao et al., 2015), accelerated 4D flow (Cheng et al., 2016). A multi–scale low–rank approach has been recently introduced by Ong and Lustig (2016) which decomposes the image into different local detail scales. Dictionary learning techniques have also been developed for MRI reconstruction in which the sparse basis is learned from the data (Caballero et al., 2014; Liu et al., 2013; Wang and Ying, 2014) and recently combined with low–rank regularization (Ravishankar et al., 2016). Initial applications of deep learning approaches have also been recently presented by Wang et al. (2016).

- Future work, page 120, second paragraph:

The wide range of methods that are being proposed for MRI reconstruction based on low–rank and PS approaches will be considered for future extensions of the developed methods specially to other MRI modalities in which the intensity of the tissues does not remain constant along time (such as perfusion studies) and for which the temporal TV does not fit as an ideal regularization term. Moreover, the inclusion of ME techniques will be studied. As an

example of this possibility, Mohsin et al. (2017) have introduced a patch–based regularization scheme in which an implicit motion correction takes place.

2 *The thesis should also be careful to point out the potential limitations of using unrealistic simulations based on DICOM images or the XCAT phantom. To avoid bias, it is important that relevant caveats are clearly stated.*

The limitations of the experiments based on synthetic data and DICOM images have been pointed out clearly and discussed in the conclusions section. Nevertheless, we understand that the reviewer may have missed the fact that in all the presented publications -with the exception of the preliminary results shown in Chapter 6- real data experiments are also included for final validation. The different kinds of data used for validation are presented in the methodology subsection to provide a general view of the procedure followed during the development of the thesis.

To this end, the following modifications have been included:

- Methodology section, page 18, second paragraph and numbered list:

The validation experiments have been realized using four different sources of data, when applicable:

1 Synthetically generated k–space data using the XCAT tool (Segars et al., 2010; Wissmann et al., 2014), in which the exact solution (i.e., the images) and the motion are known beforehand. This permits to evaluate the performance of the proposed methods both in ideal conditions and when controlled signal degradation is introduced, and for different acceleration factors. However, synthetically generated functions are in general simpler —so sparser— than real images, what facilitates their reconstruction.

2 Simulated k–space data obtained from magnitude DICOM images both from healthy subjects and patients. This permits to validate the method for images with a more realistic structure than synthetic ones and in subjects with different heart abnormalities. However, in this data phase information in the originally complex images is lost.

3 True raw k–space data obtained from Cartesian fully sampled acquisitions. This permits to validate the proposed methods in a realistic situation. Data is retrospectively undersampled to simulate different acceleration factors.

4 True raw k–space data obtained from Golden Radial acquisitions. In this approach data is continuously acquired and acceleration factors are set by setting the acquisition time or temporal resolution, when applicable.

- Limitations section, page 133, second paragraph:

As a part of the validation procedure, synthetic data generated both with numerical phantoms and from magnitude DICOM images where used in initial experiments. Even if the numerical phantom represents realistic geometries of the internal organs and their motion along both the cardiac and the respiratory cycles, the generated images are much sparser than real MRI data. Moreover, synthetic sensitivity maps are used for the multi–coil data generation, so perfect match —apart from added noise— between data and signal generation model exists. This is not true in real scenarios, in which multiple system imperfections such as gradient non-linearities, delays, errors in the estimated sensitivity maps, etc. are present. However, even taken these limitations into account, all the contributions presented in this Thesis include validation experiments with real data with the exception of the preliminary results presented in Chapter 7.

5 Minor changes recommended and modifications introduced

In the following section we describe other changes recommended by the reviewers to improve the quality of the thesis. The modifications introduced in the thesis are highlighted in blue color.

1 *A discussion of algorithm initialization and convergence issues would increase the depth of the thesis.*

In Chapter 3, section 3.4, an experiment is presented in which the robustness of the proposed algorithm is tested against very different initializations. Although no mathematical proof of convergence is provided for the optimization problem formulated, these results provide empirical evidence of the robustness of the method in this specific aspect.

This idea has been discussed more clearly in the limitations section, page 132 and 133:

> Another issue has to do with the convergence properties of the iterative reconstruction algorithm proposed, in which two optimization problems are solved iteratively. The sensitivity of the reconstruction method with respect to the initialization has been tested in Chapter 3, what provides empirical evidence of robustness against getting stacked at a local minimum far from the ideal solution. However, no mathematical proof of convergence is provided.

In the contributions section, page 132, the empirical evidence of the method being robust against differences in its initialization is pointed out:

4. Reconstruction of cine cardiac images with the proposed ME technique and the jacobian weighting term is robust against very different initialization of the algorithm.

2 *Consider whether or not the material about alpha-stable distributions is worth including in the thesis. I think the MRI content could suffice for a doctoral degree, and the thesis would be substantially more cohesive if this additional content were removed.*

The relevance of the alpha-stable distributions in biomedical image analysis and modeling in compressed sensing based recovery of sparse signals has been highlighted both in the introduction and in the future work sections. In particular, the previous expertise of the research group in the characterization of the speckle noise in ultrasound data (Vegas-Sánchez-Ferrero et al. (2012) is referenced. We consider that these points clarify the relevance of this material in the general context of the thesis. Although the application of the alpha-stable distributions to sparse signal recovery has not been tested in the work presented, its is considered as a future research line.

The specific modifications introduced follow:

- Introduction, page 3, first paragraph:

> α–stable distributions have been applied in two field specially relevant for the topic of this Thesis concerning biomedical image modeling, analysis and CS based recovery of sparse signals. Vegas-Sánchez-Ferrero et al. (2012) use them to characterize speckle noise in medical ultrasonic data and Salas-Gonzalez et al. (2013) to model white and gray matter of the brain in MRI. Li et al. (2014) use them to recover sparse signals under compressed sensing theory. Both of these proposals, in turn, have many applications on their own and the list is far from complete.

- Future work section, page 136

> Finally, in this work the tools developed for managing α–stable distributions and their capability to model biomedical images have not been explored. In particular, totally skewed α–stable distributions are well suited to model non–negative signals as proposed by Li et al. (2014), a situation that holds in other image modalities, such as CT. Moreover, recently proposed methods for radiation dose reduction in CT (Koesters et al., 2017) are based on CS in with the images are recovered from just a fraction of the originally needed projections. Therefore, the linkage between a powerful statistical signal model based on α–stable distributions and the reconstruction of low dose CT from a reduced number of projections will be considered for future research lines.

3 *When introducing alpha-stable distributions in the introduction give some examples of their uses in a couple of sentences.*

Please see the modifications introduced in the preceding point.

4 *Minor corrections and typos.*

The thesis document has been thoroughly revised and both those minor corrections indicated above and detected typos have been corrected.

Valladolid, March 29th 2017.

Javier Royuela del Val