

000 001 002 003 004 005 CONFORMAL CONFIDENCE SETS FOR BIOMEDICAL 006 IMAGE SEGMENTATION 007 008 009

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ABSTRACT

025 We develop confidence sets which provide spatial uncertainty guarantees for the
 026 output of a black-box machine learning model designed for image segmentation.
 027 To do so we adapt conformal inference to the imaging setting, obtaining thresh-
 028 olds on a calibration dataset based on the distribution of the maximum of the
 029 transformed logit scores within and outside of the ground truth masks. We prove
 030 that these confidence sets, when applied to new predictions of the model, are guar-
 031 anteed to contain the true unknown segmented mask with desired probability. We
 032 show that learning appropriate score transformations on an *independent* learning
 033 dataset before performing calibration is crucial for optimizing performance. *We*
 034 *illustrate and validate our approach on polyps colonoscopy, brain imaging datasets*
 035 *and teeth datasets. To do so we obtain the logit scores from deep neural networks*
 036 *trained for polyps, brain mask and tooth segmentation segmentation. We show*
 037 *that using using distance and other transformations of the logit scores allows us*
 038 *to provide tight inner and outer confidence sets for the true masks whilst control-*
 039 *ling the false coverage rate.*

040 1 INTRODUCTION

041 Deep neural networks promise to significantly enhance a wide range of important tasks in biomed-
 042 ical imaging. However these models, as typically used, lack formal uncertainty guarantees on their
 043 output which can lead to overconfident predictions and critical errors (Guo et al., 2017; Gupta et al.,
 044 2020). Misclassifications or inaccurate segmentations can lead to serious consequences, includ-
 045 ing misdiagnosis, inappropriate treatment decisions, or missed opportunities for early intervention
 046 (Topol, 2019). Without uncertainty quantification, medical professionals cannot rely on deep learn-
 047 ing models to provide accurate information and predictions which can limit their use in practical
 048 applications (Jungo et al., 2020).

049 In order to address this problem, conformal inference, a robust framework for uncertainty quan-
 050 tification, has become increasingly used as a means of providing prediction guarantees, offering
 051 reliable, distribution-free confidence sets for the output of neural networks which have finite sample
 052 validity. This approach, originally introduced in Papadopoulos et al. (2002); Vovk et al. (2005),
 053 has become increasingly popular due to its ability to provide rigorous statistical guarantees without
 054 making strong assumptions about the underlying data distribution or model architecture. Conformal
 055 prediction methods, in their most commonly used form - split conformal inference - work by cali-
 056 brating the predictions of the model on a held-out dataset in order to provide sets which contain the
 057 output with a given probability, see Shafer & Vovk (2008) and Angelopoulos & Bates (2021) for
 058 good introductions.

059 In the context of image segmentation, we have a decision to make at each pixel/voxel of an im-
 060 age which can lead to a large multiple testing problem. Traditional conformal methods, typically
 061 designed for scalar outputs, require adaptation to handle multiple tests and their inherent spatial
 062 dependencies. To do so Angelopoulos et al. (2021) applied conformal inference pixelwise and per-
 063 formed multiple testing correction on the resulting p -values, however this approach does not account
 064 for the complex dependence structure inherent in the images. To take advantage of this structure, in
 065 an approach analogous to the *False discovery rate (FDR)* control of (Benjamini & Hochberg, 1995),
 066 Bates et al. (2021) and Angelopoulos et al. (2024) sought to control the expected risk of a given
 067 loss function over the image and used a conformal approach to produce outer confidence sets for

054 segmented images which control the expected proportion of false negatives. Other work considering
 055 conformal inference in the context of multiple dependent hypotheses includes Marandon (2024) and
 056 Blanchard et al. (2024) who established conformal FDR control when testing for the presence of
 057 missing links in graphs.

058 In this work we argue that bounding the segmented outcome with guarantees in probability rather
 059 than on the proportion of discoveries is more informative, avoiding errors at the borders of potential
 060 growths/tumors. This is analogous to the tradeoff between *familywise error rate (FWER)* and *FDR*
 061 control in the multiple testing literature in which there is a balance between power and coverage
 062 rate, (*a correspondence which we formalize in Section A.9*). The distinction is that in medical im-
 063 age segmentation making mistakes can have potentially serious consequences Under-segmentation
 064 might cause part of the true mask to be missed, potentially leading to inadequate treatment (Jalalifar
 065 et al., 2022). Over-segmentation, on the other hand, could result in unnecessary interventions, in-
 066 creasing patient risk and healthcare costs (Gupta et al., 2020; Patz et al., 2014). Confidence sets are
 067 instead guaranteed to contain the outcome with a given level of certainty. Since the guarantees are
 068 more meaningful the problem is more difficult and existing work on conformal uncertainty quan-
 069 tification for images has thus often focused on producing sets with guarantees on the proportions
 070 of discoveries or pixel level inference rather than coverage (Bates et al. (2021), Wieslander et al.
 071 (2020), Mossina et al. (2024)) which is a stricter error criterion.

072 In order to obtain confidence sets we use a split-conformal inference approach in which we learn
 073 appropriate cutoffs, with which to threshold the output of an image segmenter, from a calibration
 074 dataset. These thresholds are obtained by considering the distribution of the maximum logit (trans-
 075 formed) scores provided by the model within and outside of the ground truth masks. This approach
 076 allows us to capture the spatial nature of the uncertainty in segmentation tasks, going beyond simple
 077 pixel-wise confidence measures. By applying these learned thresholds to new predictions, we can
 078 generate inner and outer confidence sets that are guaranteed to contain the true, unknown segmented
 079 mask with a desired probability. As we shall see, naively using the original logit scores to do so can
 080 lead to rather large and uninformative outer confidence sets but these can be greatly improved using
 081 distance transformations.

082 2 THEORY

083 2.1 SET UP

084 Let $\mathcal{V} \subset \mathbb{R}^m$, for some dimension $m \in \mathbb{N}$, be a finite set corresponding to the domain which
 085 represents the pixels/voxels/points at which we observe imaging data. Let $\mathcal{X} = \{g : \mathcal{V} \rightarrow \mathbb{R}\}$ be
 086 the set of real functions on \mathcal{V} and let $\mathcal{Y} = \{g : \mathcal{V} \rightarrow \{0, 1\}\}$ be the set of all functions on \mathcal{V} taking
 087 the values 0 or 1. We shall refer to elements of \mathcal{X} and \mathcal{Y} as images. Suppose that we observe a
 088 calibration dataset $(X_i, Y_i)_{i=1}^n$ of random images, where $X_i : \mathcal{V} \rightarrow \mathbb{R}$ represents the i th observed
 089 calibration image and $Y_i : \mathcal{V} \rightarrow \{0, 1\}$ outputs labels at each $v \in \mathcal{V}$ giving 1s at the true location
 090 of the objects in the image X_i that we wish to identify and 0s elsewhere. Let $\mathcal{P}(\mathcal{V})$ be the set of all
 091 subsets of \mathcal{V} . Given a function $f : \mathcal{X} \rightarrow \mathcal{X}$, we shall write $f(X, v)$ to denote $f(X)(v)$ for all $v \in \mathcal{V}$.

092 Let $s : \mathcal{X} \rightarrow \mathcal{X}$ be a score function - trained on an independent dataset - such that given an image
 093 pair $(X, Y) \in \mathcal{X} \times \mathcal{Y}$, $s(X)$ is a score image in which $s(X, v)$ is intended to be higher at the $v \in \mathcal{V}$
 094 for which $Y(v) = 1$. The score function can for instance be the logit scores obtained from applying
 095 a deep neural network image segmentation method to the image X . Given $X \in \mathcal{X}$, let $\hat{M}(X) \in \mathcal{Y}$
 096 be the predicted mask given by the model which is assumed to be obtained using the scores $s(X)$.

097 In what follows we will use the calibration dataset to construct confidence functions $I, O : \mathcal{X} \rightarrow$
 098 $\mathcal{P}(\mathcal{V})$ such that for a new image pair (X, Y) , given error rates $\alpha_1, \alpha_2 \in (0, 1)$ we have

$$099 \quad \mathbb{P}(I(X) \subseteq \{v \in \mathcal{V} : Y(v) = 1\}) \geq 1 - \alpha_1, \tag{1}$$

$$100 \quad \text{and } \mathbb{P}(\{v \in \mathcal{V} : Y(v) = 1\} \subseteq O(X)) \geq 1 - \alpha_2. \tag{2}$$

101 Here $I(X)$ and $O(X)$ serve as inner and outer confidence sets for the location of the true segmented
 102 mask. Their interpretation is that, up to the guarantees provided by the probabilistic statements (1)
 103 and (2), we can be sure that for each $v \in I(X)$, $Y(v) = 1$ or that for each $v \notin O(X)$, $Y(v) = 0$.
 104 Joint control over the events can also be guaranteed, either via sensible choices of α_1 and α_2 or by
 105 using the joint distribution of the maxima of the logit scores - see Section 2.3.

In order to establish conformal confidence results we shall require the following exchangeability assumption.

Assumption 1. Given a new random image pair, (X_{n+1}, Y_{n+1}) , suppose that $(X_i, Y_i)_{i=1}^{n+1}$ is an exchangeable sequence of random image pairs in the sense that

$$\{(X_1, Y_1), \dots, (X_{n+1}, Y_{n+1})\} =_d \{(X_{\sigma(1)}, Y_{\sigma(1)}), \dots, (X_{\sigma(n+1)}, Y_{\sigma(n+1)})\}$$

for all permutations $\sigma \in S_{n+1}$. Here $=_d$ denotes equality in distribution and S_{n+1} is the group of permutations of the integers $\{1, \dots, n+1\}$.

Exchangeability or a variant is a standard assumption in the conformal inference literature (Angelopoulos & Bates, 2021) and facilitates coverage guarantees. It holds for instance if we assume that the collection $(X_i, Y_i)_{i=1}^{n+1}$ is an i.i.d. sequence of image pairs but is more general and in principle allows for other dependence structures.

2.2 MARGINAL CONFIDENCE SETS

In order to construct conformal confidence sets let $f_I, f_O : \mathcal{X} \rightarrow \mathcal{X}$ be inner and outer transformation functions and for each $1 \leq i \leq n+1$, let $\tau_i = \max_{v \in \mathcal{V}: Y_i(v)=0} f_I(s(X_i), v)$ and $\gamma_i = \max_{v \in \mathcal{V}: Y_i(v)=1} -f_O(s(X_i), v)$ be the maxima of the function transformed scores over the areas at which the true labels equal 0 and 1 respectively. We will require the following assumption on the scores and the transformation functions.

Assumption 2. (Independence of scores) $(X_i, Y_i)_{i=1}^{n+1}$ is independent of the functions s, f_O, f_I .

Given this we construct confidence sets as follows.

Theorem 2.1. (*Marginal inner set*) Under Assumptions 1 and 2, given $\alpha_1 \in (0, 1)$, let

$$\lambda_I(\alpha_1) = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n \mathbb{1}[\tau_i \leq \lambda] \geq \frac{\lceil (1 - \alpha_1)(n + 1) \rceil}{n} \right\},$$

and define $I(X) = \{v \in \mathcal{V} : f_I(s(X), v) > \lambda_I(\alpha_1)\}$. Then,

$$\mathbb{P}(I(X_{n+1}) \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\}) \geq 1 - \alpha_1. \quad (3)$$

Proof. Under Assumptions 1 and 2, exchangeability of the image pairs implies exchangeability of the sequence $(\tau_i)_{i=1}^{n+1}$. In particular, $\lambda_I(\alpha_1)$ is the upper α_1 quantile of the distribution of $(\tau_i)_{i=1}^n \cup \{\infty\}$ and so, by Lemma 1 of Tibshirani et al. (2019), it follows that

$$\mathbb{P}(\tau_{n+1} \leq \lambda_I(\alpha_1)) \geq 1 - \alpha_1.$$

Now consider the event that $\tau_{n+1} \leq \lambda_I(\alpha_1)$. On this event, $f_I(s(X_{n+1}), v) \leq \lambda_I(\alpha_1)$ for all $v \in \mathcal{V}$ such that $Y_{n+1}(v) = 0$. As such, given $u \in \mathcal{V}$ such that $f_I(s(X_{n+1}), u) > \lambda_I(\alpha_1)$, we must have $Y_{n+1}(u) = 1$ and so $I(X_{n+1}) \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\}$. It thus follows that

$$\mathbb{P}(I(X_{n+1}) \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\}) \geq \mathbb{P}(\tau_{n+1} \leq \lambda_I(\alpha_1)) \geq 1 - \alpha_1.$$

□

For the outer set we have the following analogous result.

Theorem 2.2. (*Marginal outer set*) Under Assumptions 1 and 2, given $\alpha_2 \in (0, 1)$, let

$$\lambda_O(\alpha_2) = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n \mathbb{1}[\gamma_i \leq \lambda] \geq \frac{\lceil (1 - \alpha_2)(n + 1) \rceil}{n} \right\},$$

and define $O(X) = \{v \in \mathcal{V} : -f_O(s(X), v) \leq \lambda_O(\alpha_2)\}$. Then,

$$\mathbb{P}(\{v \in \mathcal{V} : Y_{n+1}(v) = 1\} \subseteq O(X_{n+1})) \geq 1 - \alpha_2. \quad (4)$$

Proof. Arguing as in the proof of Theorem 2.1, it follows that $\mathbb{P}(\gamma_{n+1} \leq \lambda_O(\alpha_2)) \geq 1 - \alpha_2$. Now on the event that $\gamma_{n+1} \leq \lambda_O(\alpha_2)$ we have $-f_O(s(X_{n+1}), v) \leq \lambda_O(\alpha_2)$ for all $v \in \mathcal{V}$ such that $Y_{n+1}(v) = 1$. As such, given $u \in \mathcal{V}$ such that $-f_O(s(X_{n+1}), u) > \lambda_O(\alpha_2)$, we must have $Y_{n+1}(u) = 0$ and so $O(X)^C \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 0\}$. The result then follows as above. □

Remark 2.3. We have used the maximum over the transformed scores in order to combine score information on and off the ground truth masks. The maximum is a natural combination function in imaging and is commonly used in the context of multiple testing (Worsley et al., 1992). However the theory above is valid for any increasing combination function. We show this in Appendix A.1 where we establish generalized versions of these results.

Remark 2.4. Inner and outer coverage can also be viewed as a special case of conformal risk control with an appropriate choice of loss function. We can thus instead establish coverage results as a corollary to risk control, see Appendix A.2 for details. This amounts to an alternative proof of the results as the proof of the validity of risk control is different though still strongly relies on exchangeability.

2.3 JOINT CONFIDENCE SETS

Instead of focusing on marginal control one can instead spend all of the α available to construct sets which have a joint probabilistic guarantees. This gain comes at the expense of a loss of precision. The simplest means of constructing jointly valid confidence sets is via the marginal sets themselves.

Corollary 2.5. (Joint from marginal) Assume Assumptions 1 and 2 hold and given $\alpha \in (0, 1)$ and $\alpha_1, \alpha_2 \in (0, 1)$ such that $\alpha_1 + \alpha_2 \leq \alpha$, define $I(X)$ and $O(X)$ as in Theorems 2.1 and 2.2. Then

$$\mathbb{P}(I(X_{n+1}) \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\} \subseteq O(X_{n+1})) \geq 1 - \alpha. \quad (5)$$

Alternatively joint control can be obtained using the joint distribution of the maxima of the transformed logit scores as follows.

Theorem 2.6. (Joint coverage) Assume that Assumption 1 and 2 hold. Given $\alpha \in (0, 1)$, define

$$\lambda(\alpha) = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n \mathbb{1}[\max(\tau_i, \gamma_i) \leq \lambda] \geq \frac{\lceil (1-\alpha)(n+1) \rceil}{n} \right\}.$$

Let $O(X) = \{v \in \mathcal{V} : -f_O(s(X), v) \leq \lambda(\alpha)\}$ and $I(X) = \{v \in \mathcal{V} : f_I(s(X), v) > \lambda(\alpha)\}$. Then,

$$\mathbb{P}(I(X_{n+1}) \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\} \subseteq O(X_{n+1})) \geq 1 - \alpha. \quad (6)$$

Proof. Exchangeability of the image pairs implies exchangeability of the sequence $(\tau_i, \gamma_i)_{i=1}^{n+1}$. Moreover on the event that $\max(\tau_{n+1}, \gamma_{n+1}) \leq \lambda(\alpha)$ we have $\tau_{n+1} \leq \lambda(\alpha)$ and $\gamma_{n+1} \leq \lambda(\alpha)$ so the result follows via a proof similar to that of Theorems 2.1 and 2.2. \square

Remark 2.7. The advantage of Corollary 2.5 is that the resulting inner and outer sets provide pivotal inference - not favouring one side or the other - which can be important when the distribution of the score function is asymmetric. Moreover the levels α_1 and α_2 can be used to provide a greater weight to either inner or outer sets whilst maintaining joint coverage. Theorem 2.6 may instead be useful when there is strong dependence between τ_{n+1} and γ_{n+1} . However, when this dependence is weak, scale differences in the scores can lead to a lack of pivotality. This can be improved by appropriate choices of the score transformations f_I and f_O however in practice it may be simpler to construct joint sets using Corollary 2.5.

2.4 OPTIMIZING SCORE TRANSFORMATIONS

The choice of score transformations f_I and f_O is extremely important and can have a large impact on the size of the conformal confidence sets. The best choice depends on both the distribution of the data and on the nature of the output of the image segmentor used to calculate the scores. We thus recommend setting aside a learning dataset independent from both the calibration dataset, used to compute the conformal thresholds, and the test dataset. This approach was used in Sun & Yu (2024) to learn the best copula transformation for combining dependent data streams.

In order to make efficient use of the data available, the learning dataset can in fact contain some or all of the data used to train the image segmentor. This data is assumed to be independent of the calibration and test data and so can be used to learn the best score transformations without compromising subsequent validity. The advantage of doing so is that less additional data needs to be set aside or collected for the purposes of learning a score function. Moreover it allows for additional

216 data to be used to train the model resulting in better segmentation performance. The disadvantage is
 217 that machine learning models typically overfit their training data meaning that certain score functions
 218 may appear to perform better on this data than they do in practice. The choice of whether to include
 219 training data in the learning dataset thus depends on the quantity of data available and the quality of
 220 the segmentation model.

221 A score transformation that we will make particular use of in Section 3 is based on the distance
 222 transformation which we define as follows. Given $\mathcal{A} \subseteq \mathcal{V}$, let $E(\mathcal{A})$ be the set of points on the
 223 boundary of \mathcal{A} obtained using the marching squares algorithm (Maple, 2003). Given a distance
 224 metric ρ define the distance transformation $d_\rho : \mathcal{P}(\mathcal{V}) \times \mathcal{V} \rightarrow \mathbb{R}$, which sends $\mathcal{A} \in \mathcal{P}(\mathcal{V})$ and $v \in \mathcal{V}$
 225 to

$$d_\rho(\mathcal{A}, v) = \text{sign}(\mathcal{A}, v) \min\{\rho(v, e) : e \in E(\mathcal{A})\},$$

226 where $\text{sign}(\mathcal{A}, v) = 1$ if $v \in \mathcal{A}$ and equals -1 otherwise. The function d_ρ is an adaption of
 227 the distance transform of Borgefors (1986) which provides positive values within the set \mathcal{A} and
 228 negative values outside of \mathcal{A} . *Moreover define the Hausdorff distance between two sets $\mathcal{A}, \mathcal{B} \subseteq \mathcal{V}$
 229 as $H_\rho(\mathcal{A}, \mathcal{B}) = \max\{\sup_{a \in \mathcal{A}} \inf_{b \in \mathcal{B}} \rho(a, b), \sup_{b \in \mathcal{B}} \inf_{a \in \mathcal{A}} \rho(b, a)\}$, The following result shows
 230 that transforming the scores using the distance transformation ensures that accurate segmentation
 231 provides precise confidence sets. See Section A.3 for a proof.*

232 **Theorem 2.8.** *For each $v \in \mathcal{V}$, let $f_O(s(X), v) = d_\rho(\hat{M}(X), v)$ and define $O(X)$ as in Section
 233 2.2. Suppose that $H(\hat{M}(X_i), Y_i) \leq k$, some $k \in \mathbb{R}$, for all $i \in J$, for some $J \subseteq \{1, \dots, n\}$ such
 234 that $\frac{|J|}{n} > 1 - \alpha_2$. Then $H(\hat{M}(X_{n+1}), O(X_{n+1})) \leq k$. In particular if $H(\hat{M}(X_{n+1}), Y_{n+1}) \leq k$,
 235 then it follows that $H(O(X_{n+1}), Y_{n+1}) \leq 2k$.*

236 A similar result holds for the inner confidence sets, see Theorem A.4. Note that a corresponding
 237 result is not true for the untransformed logit scores, see Figure A20.

243 2.5 CONSTRUCTING CONFIDENCE SETS FROM BOUNDING BOXES

244 Existing work on conformal inner and outer confidence sets, which aim to provide coverage of
 245 the entire ground truth mask with a given probability, has primarily focused on bounding boxes
 246 (de Grancey et al., 2022; Andéol et al., 2023; Mukama et al., 2024). These papers adjust for mul-
 247 tiple comparisons over the 4 edges of the bounding box, doing so conformally by comparing the
 248 distance between the predicted bounding box and the bounding box of the ground truth mask. These
 249 approaches provide box-wise coverage by aggregating the predictions over all objects within all of
 250 the calibration images, often combining multiple bounding boxes per image. However, as observed
 251 in Section 5 of de Grancey et al. (2022), doing so violates exchangeability which is needed for valid
 252 conformal inference, as there is dependence between the objects within each image. Instead image-
 253 wise coverage can be provided without violating exchangeability by treating the union of the boxes
 254 as the ground truth image (de Grancey et al., 2022; Andéol et al., 2023).

255 We establish the validity of a version of the image-wise max-additive method of Andéol et al. (2023)
 256 (adapted to provide coverage of the ground truth) as a corollary to our results, see Appendix A.4.
 257 In this approach we define bounding box scores based on the chessboard distance transformation
 258 to the inner and outer predicted masks and use these scores to provide conformal confidence sets.
 259 Validity then follows as a consequence of the results above as we show in Corollaries A.6 and A.7.
 260 We compare to this approach in our experiments below. Targeting bounding boxes does not directly
 261 target the mask itself and so the resulting confidence sets are typically conservative.

263 3 APPLICATION TO POLYPS SEGMENTATION

264 In order to illustrate and validate our approach we consider the problem of polyps segmentation. To
 265 do so we use the same dataset as in Angelopoulos et al. (2024) in which 1798 polyps images, with
 266 available ground truth masks were combined from 5 open-source datasets (Pogorelov et al. (2017),
 267 Borgli et al. (2020) Bernal et al. (2012), Silva et al. (2014)). Logit scores were obtained for these
 268 images using the parallel reverse attention network (PraNet) model (Fan et al., 2020).

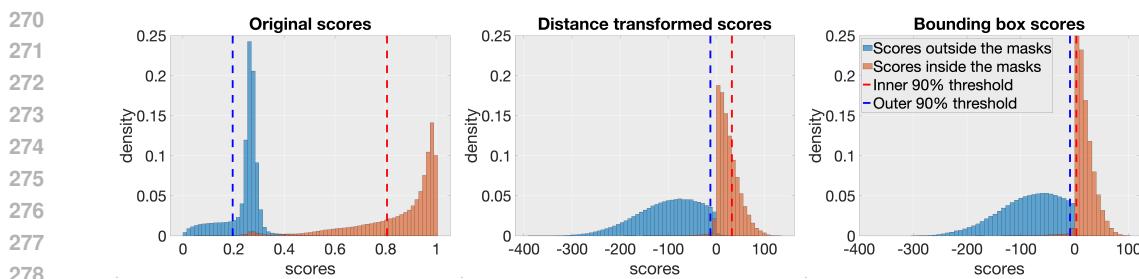


Figure 1: Histograms of the distribution of the scores over the whole image within and outside the ground truth masks. Thresholds obtained for the marginal 90% inner and outer confidence sets, obtained based on quantiles of the distribution of $(\tau_i)_{i=1}^n$ and $(\gamma_i)_{i=1}^n$, are displayed in red and blue.

3.1 CHOOSING A SCORE TRANSFORMATION

In order to optimize the size of our confidence sets we set aside 298 of the 1798 polyps images to form a learning dataset on which to choose the best score transformations. Importantly as the learning dataset is independent of the *1500 images which we set aside*, we can study it as much as we like without compromising the validity of the follow-up analyses in Sections 3.2. In particular in this section we shall use the learning dataset to both calibrate and study the results, in order to maximize the amount of important information we can learn from it.

The score transformations we considered were the identity (after softmax transformation) and distance transformations of the predicted masks: taking $f_I(s(X), v) = f_O(s(X), v) = d_\rho(\hat{M}(X), v)$, where ρ is the Euclidean metric. We also compare to the results of using the bounding box transformations $f_I = b_I$ and $f_O = b_O$ which correspond to transforming the predicted bounding box using a distance transformation based on the chessboard metric and are defined formally in Appendix A.4. For the purposes of plotting we used the combined bounding box scores defined in Definition A.5.

From the histograms in Figure 1 we can see that thresholding the logit scores at the inner threshold well separates the data. However this is not the case for the outer threshold for which the data is better separated using the distance transformed and bounding box scores. Figure 2 shows PraNet scores for 2 typical examples, along with surface plots of the transformed scores and corresponding 90% marginal confidence regions (with thresholds obtained from calibrating over the learning dataset). From these we see that PraNet typically assigns a high softmax score to the polyps regions which decreases in the regions directly around the boundary before returning to a higher level away from the polyps. This results in tight inner sets but large outer sets as the model struggles to identify where the polyps ends. Instead the distance transformed and bounding box scores are much better at providing outer bounds on the polyps, with distance transformed scores providing a tighter outside fit. Additional examples are shown in Figures A8 and A9 and have the same conclusion.

Based on the results of the learning dataset we decided to combine the best of the approaches for the inner and outer sets respectively for the inference in Section 3.2, taking f_I to be the identity and f_O to be the distance transformation of the predicted mask in order to optimize performance. We can also use the learning dataset to determine how to weight the α used to obtain joint confidence sets. A ratio of 4 to 1 seems appropriate here in light of the fact that in this dataset identifying where a given polyps ends appears to be more challenging than identifying pixels where we are sure that there is a polyps. To achieve joint coverage of 90% this involves taking $\alpha_1 = 0.02$ and $\alpha_2 = 0.08$.

3.2 ILLUSTRATING THE PERFORMANCE OF CONFORMAL CONFIDENCE SETS

In order to illustrate the full extent of our methods in practice we divide the *remaining 1500* images at random into 1000 for conformal calibration, and 500 for testing. The resulting conformal confidence sets for 10 example images from the test dataset are shown in Figure 3, with inner sets obtained using the untransformed logit scores and outer sets using the distance transformed scores. The inner sets are shown in red and represent regions where we can have high confidence of the presence of polyps. The outer sets are shown in blue and represent regions in which the polyps may be. The ground truth mask for each polyps is shown in yellow and can be compared to the original images. In

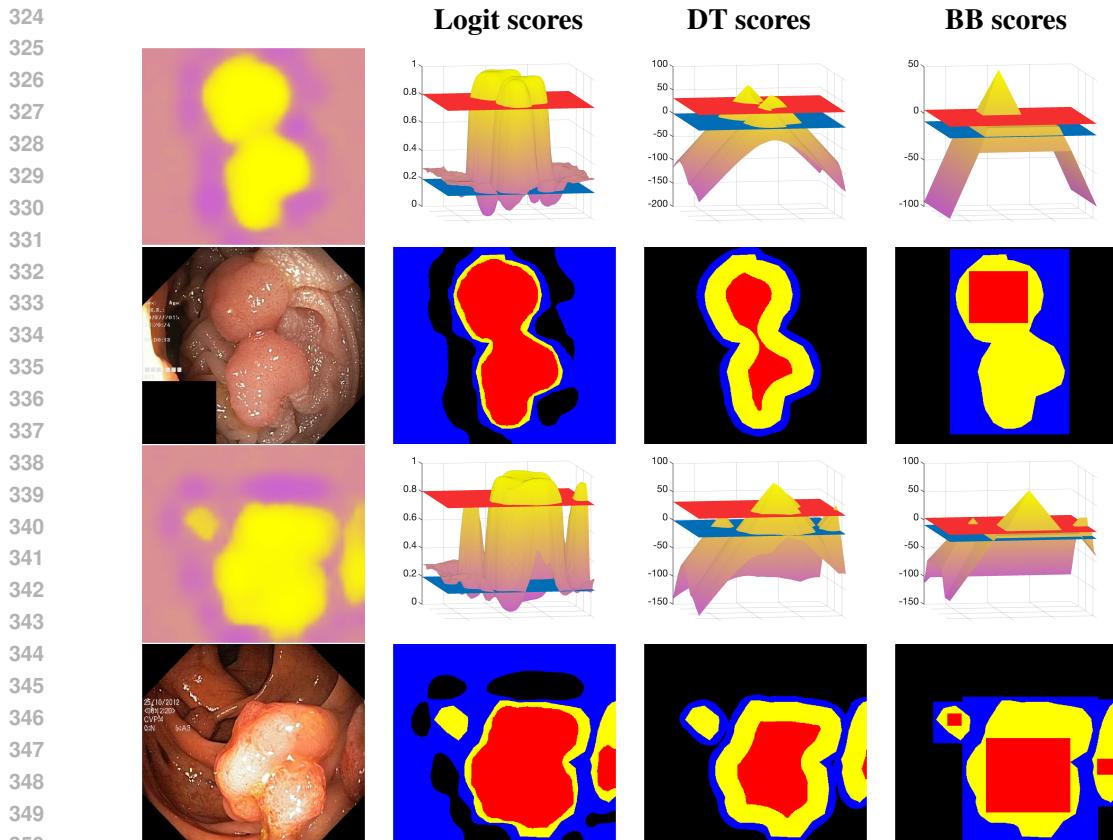


Figure 2: Illustrating the performance of the different score transformations on the learning dataset. We display 2 example polyps images and present the results of each in 8 panels. These panels are as follows. Bottom left: the original image of the polyps. Top Left: an intensity plot of the scores obtained from PraNet with purple/yellow indicating areas of lower/higher assigned probability. For the remaining panels, 3 different score transformations are shown which from left to right are the untransformed logit scores, distance transformed (DT) scores $d_\rho(\hat{M}(X), v)$ and bounding box (BB) scores (obtained using the combined bounding box score b_M defined in Definition A.5). In each of the panels on the top row a surface plot of the transformed PraNet scores is shown, along with the conformal thresholds which are used to obtain the marginal 90% inner and outer confidence sets. These thresholds are illustrated via red and blue planes respectively and are obtained over the learning dataset. The panels on the bottom row of each example show the corresponding conformal confidence sets. Here the inner set is shown in red, plotted over the ground truth mask of the polyps, shown in yellow, plotted over the outer set which is shown in blue. The outer set contains the ground truth mask which contains the inner set in all examples. From these figures we see that the logit scores provide tight inner confidence sets and the distance transformed scores instead provide tight outer confidence sets. The conclusion from the learning dataset is therefore that it makes sense to combine these two score transformations.

each of the examples considered the ground truth is bounded from within by the inner set and from without by the outer set. Results for confidence sets based on the logit and bounding box scores as well as additional examples are available in Figures A10 and A11. Confidence sets can also be provided for the bounding boxes themselves if that is the object of interest, see Figure A12. Joint 90% confidence sets are displayed in Figure A13, from which we can see that with alpha-weighting (i.e. taking $\alpha_1 = 0.02$ and $\alpha_2 = 0.08$) we are able to obtain joint confidence sets which are still relatively tight.

These results collectively show that we can provide informative confidence bounds for the location of the polyps and allow us to use the PraNet segmentation model with uncertainty guarantees. From Figure 3 we can see that the method, which combines the logit and the distance transformed scores, effectively delineates polyps regions. These results also help to make us aware of the limitations of

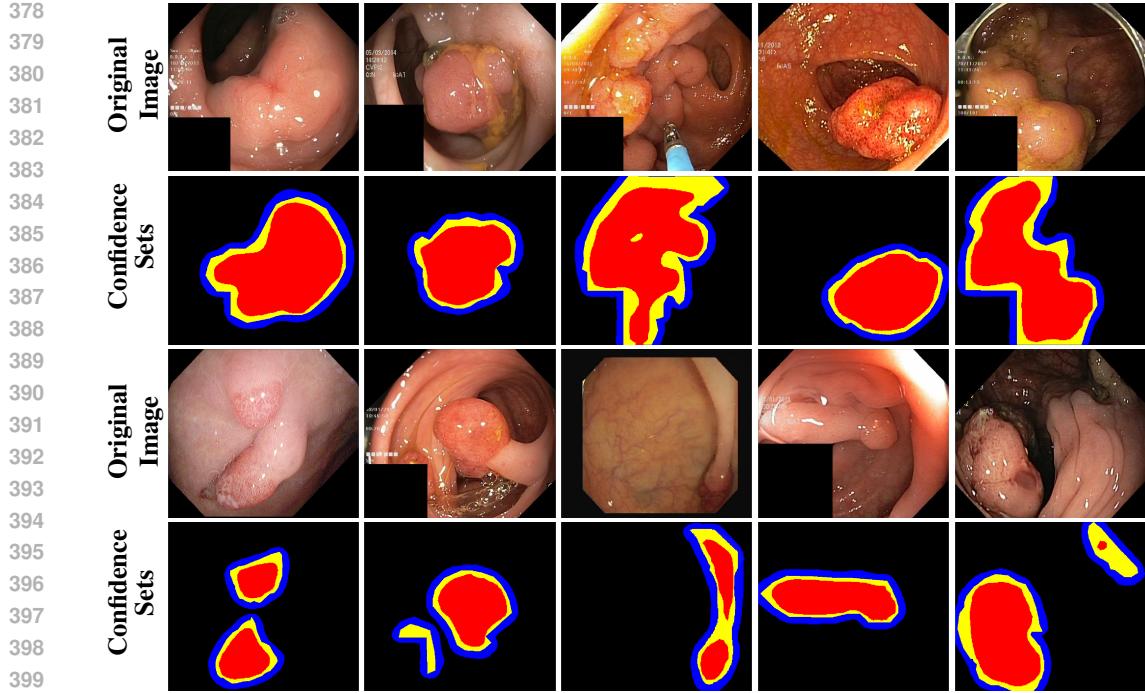


Figure 3: Conformal confidence sets for the polyps data. For each set of polyps images the top row shows the original endoscopic images with visible polyps and the second row presents the marginal 90% confidence sets, with ground truth masks shown in yellow. The inner sets and outer sets are shown in red and blue, obtained using the identity and distance transforms respectively. The figure shows the benefits of combining different score transformations for the inner and outer sets and illustrates the method’s effectiveness in accurately identifying polyp regions whilst providing informative spatial uncertainty bounds.

the model, allowing medical practitioners to follow up on outer sets which do not contain inner sets in order to determine whether a polyps is present. Improved uncertainty quantification would require an improved segmentation model.

More precise results can be obtained at the expense of probabilistic guarantees, see Figures A14 and A15. A trade off must be made between precision and confidence. The most informative confidence level can be determined in advance based on the learning dataset and the desired type of coverage.

3.3 MEASURING THE COVERGE RATE

In this section we run validations to evaluate the false coverage rate of our approach. To do so we take the *1500 images which we set aside* and run 1000 validations, in each validation dividing the data into 1000 calibration and 500 test images. In each division we calculate the conformal confidence sets using the different score transformations, based on thresholds derived from the calibration dataset, and evaluate the coverage rate on the test dataset. We average over all 1000 validations and present the results in Figure 4. Histograms for the 90% coverage obtained over all validation runs are shown in Figure A16.

From these results we can see that for all the approaches the coverage rate is controlled at or above the nominal level as desired. Using the bounding box scores results in slight over coverage at lower confidence levels. This is likely due to the discontinuities in the score functions b_I and b_O .

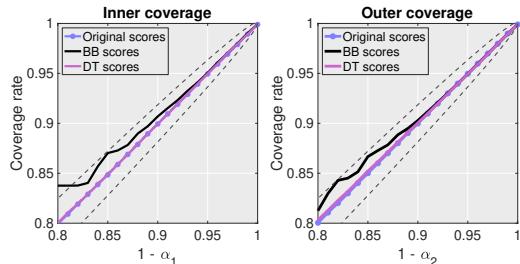
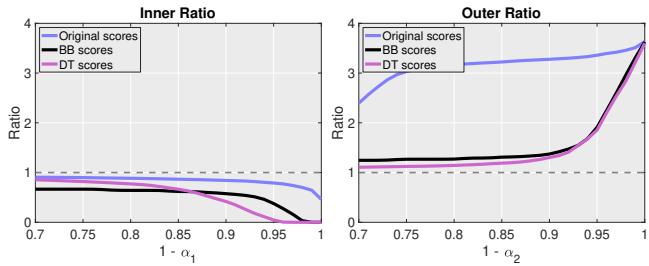


Figure 4: Coverage levels of the inner and outer sets averaged over 1000 validations for the original, distance transformed (DT) and bounding box (BB) scores. *95% uncertainty bands are shown with the dashed grey lines.*

432 **3.4 COMPARING THE EFFICIENCY OF THE BOUNDS**
 433

434 In this section we compare the efficiency of the confidence sets based on the different score trans-
 435 formations. To do so we run 1000 validations in each dividing and calibrating as in Section 3.3.



446 Figure 5: Measuring the efficiency of the bound using the ratio
 447 of the diameter of the coverage set to the diameter of the true
 448 mask. The closer the ratio is to one the better. Higher
 449 coverage rates lead to a lower efficiency. The logit scores
 450 provide the most efficient inner sets and the distance trans-
 451 formed scores provide the most efficient outer sets.

452 getting the proportion of the entire image which is under/over covered by the respective confidence
 453 sets. The results are shown in Figure A17 and can be interpreted similarly.

455 **4 APPLICATION TO BRAIN IMAGING SEGMENTATION**
 456

457 *As a second application we con-
 458 sider the task of skull stripping.
 459 This task consists of segmenting
 460 the brain given an Magnetic
 461 resonance image of a hu-
 462 man head. For image seg-
 463 mentation we use the HD-BET
 464 (Isensee et al., 2019) neural net-
 465 work model which was trained
 466 on dataset of 1,568 subjects and
 467 has quickly become the defacto
 468 method of performing brain mask
 469 segmentation. In order to ap-
 470 ply our methods in this setting
 471 we combine data from 3 pub-
 472 lic datasets (LPBA40, NFBS, and
 473 CC-359) resulting in 524 brain images in total. This data is independent from the data used to train
 474 HD-BET, see e.g. (Isensee et al., 2019). We divide this data into 50 subjects to make up a learning
 475 dataset, use 300 subjects to perform calibration and use the remaining subjects for testing.*

476 *Based on the results of the learning dataset, see Appendix A.6.1, we see that the distance transformed
 477 scores perform best for constructing both inner and outer confidence sets. The naive approach of
 478 using the untransformed logit scores performs very poorly for both inner and outer sets. Calibrating
 479 thresholds for the distance transformed scores using the calibration dataset and applying to the
 480 images from the testing dataset we obtain informative inner and outer confidence sets, as shown in
 481 Figure 6. Validating as in Section 3.3, we see that the false coverage rate is controlled to the nominal
 482 level, see Section A.6.4.*

483 **5 APPLICATION TO TEETH SEGMENTATION**
 484

485 *As a third application we consider the problem of teeth segmentation. We use a dataset (released by
 486 Zhang et al. (2023)) consisting of scans of the teeth of 598 subjects and train a U-net based GAN
 487 network using 400 subjects (following Hoshme (2024)). We divide the remaining 198 subjects into
 488 170 to use as calibration data and 28 to use as a test dataset. We use the original training data as a*

For each run we compute the ratio between the diameter of the inner set and the diameter of the ground truth mask and average this ratio over the 500 test images. In order to make a smooth curve we average this quantity over all 1000 runs. A similar calculation is performed for the outer set. The results are shown in Figure 5. They show that the inner confidence sets produced by using the logit scores are the most efficient. Instead, for the outer set, the distance transformed scores perform best. These results match the observations of Sections 3.1 and 3.2.

We repeat this procedure instead targeting the proportion of the entire image which is under/over covered by the respective confidence sets. The results are shown in Figure A17 and can be interpreted similarly.

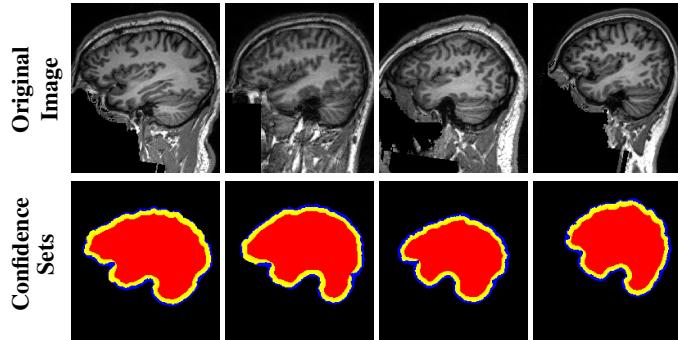


Figure 6: *Inner and outer confidence sets for brain mask segmentation: both computed using the distance trans-
 formed scores. The true mask is shown in yellow.*

learning dataset (note that this is independent of the calibration dataset so does not affect validity). We tried a variety of score transformations including distance transformations and smoothing, see Section A.7. Based on the learning data we chose the distance transformation for the outer sets and smoothing with a full width at half maximum (FWHM) of 2 pixels for the inner set. Calibrating thresholds on the calibration dataset and applying to the test data we obtain the results shown in Figure 7. Moreover, validating as in Section 3.3, we show that the false coverage rate is controlled to the nominal level in practice, see Section A.7.4.



Figure 7: Inner and outer confidence sets for teeth segmentation computed using scores smoothed with 2 pixel FWHM and distance transformed scores respectively. The true mask is shown in yellow.

6 DISCUSSION

In this work, we have developed conformal confidence sets which offer probabilistic guarantees for the output of a black box image segmentation model and provide tight bounds. Our work helps to address the lack of formal uncertainty quantification in the application of deep neural networks to medical imaging which has limited the reliability and adoption of these models in practice. *Confidence sets provide informative spatial bounds on the expected output and ensure that we are not overconfident about our model predictions.*

The use of the distance transformed scores *was important in providing tight outer confidence bounds in all applications considered* as the original neural network is by itself unable to reliably determine where the true masks end with certainty. The distance transformation penalizes regions away from the predicted mask, allowing the true mask to be distinguished from the background. In other datasets and model settings, other transformations may be appropriate. We saw for instance that smoothing the scores can be beneficial and allow the model to boost power using spatial information. As such we strongly recommend the use of a learning dataset to learn the best transformation and maximize the precision of the resulting confidence bounds.

The use of improved neural networks which can better separate the scores within and outside the ground truth masks would lead to more precise confidence sets and optimizing this is an important area of research.

The confidence sets we develop in this paper are related in spirit to work on uncertainty quantification for spatial excursion sets (Chen et al. (2017), Bowring et al. (2019), Mejia et al. (2020)). These approaches instead assume that multiple observations from a signal plus noise model are observed and perform inference on the underlying signal rather than prediction. Unlike conformal inference these approaches rely on central limit theorems or distributional assumptions in order to provide spatial confidence regions with asymptotic coverage guarantees.

Matlab code to implement the methods of this paper and a demo on a downsampled version of the data is available in the supplementary material. The code is very fast: calculating inner and outer thresholds (over the 1000 images in the calibration set) requires approximately 0.03 seconds on the downsampled polyps data on a standard laptop (Apple M3 chip with 16 GB RAM) and 2.64 seconds for the original polyps dataset. *This fast performance is due to our observation that it is sufficient to rely on quantiles of the maximum scores within and outside the mask, meaning we don't have to rely on binary search to obtain the conformal prediction threshold.*

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702 **A APPENDIX**

704 **A.1 OBTAINING CONFORMAL CONFIDENCE SETS WITH INCREASING COMBINATION**
 705 **FUNCTIONS**

707 As discussed in Remark 2.3 the results of Sections 2.2 and 2.3 can be generalized to a wider class
 708 of combination functions.

709 **Definition A.1.** We define a suitable combination function to be a function $C : \mathcal{P}(\mathcal{V}) \times \mathcal{X} \rightarrow \mathbb{R}$
 710 which is increasing in the sense that for all sets $\mathcal{A} \subseteq \mathcal{V}$ and each $v \in \mathcal{A}$, $C(v, X) \leq C(\mathcal{A}, X)$ for
 711 all $X \in \mathcal{X}$.

712 The maximum is a suitable combination function since $X(v) = \max_{v \in \{v\}} X(v) \leq \max_{v \in \mathcal{A}} X(v)$.
 713 As such this framework directly generalizes the results of the main text.

714 We can construct generalized marginal confidence sets as follows.

716 **Theorem A.2.** (*Marginal inner set*) Under Assumptions 1 and 2, given $\alpha_1 \in (0, 1)$, define

$$717 \quad \lambda_I(\alpha_1) = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n 1 [C(\{v \in \mathcal{V} : Y_i(v) = 1\}, f_I(s(X_i))) \leq \lambda] \geq \frac{\lceil (1 - \alpha_1)(n + 1) \rceil}{n} \right\},$$

720 for a suitable combination function C , and define $I(X) = \{v \in \mathcal{V} : C(v, f_I(s(X))) > \lambda_I(\alpha_1)\}$.
 721 Then,

$$722 \quad \mathbb{P}(I(X_{n+1}) \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\}) \geq 1 - \alpha_1. \quad (7)$$

723 The proof follows that of Theorem 2.1. The key observation is that for any suitable combination
 724 function C , given $\lambda \in \mathbb{R}$, $\mathcal{A} \subseteq \mathcal{V}$ and $X \in \mathcal{X}$, $C(\mathcal{A}, X) \leq \lambda$ implies that $C(v, X) \leq \lambda$. This is the
 725 relevant property of the maximum which we used for the results in the main text. For the outer set
 726 we similarly have the following.

727 **Theorem A.3.** (*Marginal outer set*) Under Assumptions 1 and 2, given $\alpha_2 \in (0, 1)$, define

$$728 \quad \lambda_O(\alpha_2) = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n 1 [C(\{v \in \mathcal{V} : Y_i(v) = 0\}, -f_O(s(X_i))) \leq \lambda] \geq \frac{\lceil (1 - \alpha_2)(n + 1) \rceil}{n} \right\}.$$

731 for a suitable combination function C , and let $O(X) = \{v \in \mathcal{V} : C(v, -f_O(s(X))) \leq \lambda_O(\alpha_2)\}$.
 732 Then,

$$733 \quad \mathbb{P}(\{v \in \mathcal{V} : Y_{n+1}(v) = 1\} \subseteq O(X_{n+1})) \geq 1 - \alpha_2. \quad (8)$$

734 Joint results can be analogously obtained.

736 **A.2 OBTAINING CONFIDENCE SETS FROM RISK CONTROL**

738 We can alternatively establish Theorems 2.1 and A.2 using an argument from risk control (Angelopoulos et al., 2024). In particular, given an image pair (X, Y) and $\lambda \in \mathbb{R}$, let

$$740 \quad I_\lambda(X) = \{v \in \mathcal{V} : f_I(s(X), v) > \lambda\}.$$

741 Define a loss function, $L : \mathcal{P}(\mathcal{V}) \times \mathcal{Y} \rightarrow \mathbb{R}$ which sends (X, Y) to

$$742 \quad L(I_\lambda(X), Y) = 1 [I_\lambda(X) \not\subseteq \{v \in \mathcal{V} : Y(v) = 1\}].$$

743 For $i = 1, \dots, n + 1$, let $L_i(\lambda) = L(I_\lambda(X_i), Y_i)$. Arguing as in the proof of Theorem 2.1 it follows
 744 that $L_i(\lambda) = 1[\tau_i > \lambda]$. Then applying Theorem 1 of Angelopoulos et al. (2024) it follows that

$$745 \quad \mathbb{E}[L_{n+1}(\hat{\lambda})] \leq \alpha_1,$$

747 where $\hat{\lambda} = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n L_i(\lambda) \leq \alpha_1 - \frac{1 - \alpha_1}{n} \right\}$. Arguing as in Appendix A of (Angelopoulos
 748 et al., 2024) it follows that

$$749 \quad \hat{\lambda} = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n 1 [\tau_i \leq \lambda] \geq \frac{\lceil (1 - \alpha_1)(n + 1) \rceil}{n} \right\} = \lambda_I(\alpha_1),$$

752 and so $I(X) = I_{\hat{\lambda}}(X)$. As such

$$753 \quad \mathbb{P}(I(X_{n+1}) \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\}) = 1 - \mathbb{E}[L_{n+1}(\hat{\lambda})] \geq 1 - \alpha_1, \quad (9)$$

754 and we recover the desired result. Arguing similarly it is possible to establish a proof of Theorem
 755 2.2.

756 A.3 CHARACTERIZING THE RELATIONSHIP BETWEEN HAUSSDORFF DISTANCE AND THE
 757 DISTANCE TRANSFORMED SCORES
 758

759 *In this section we provide a proof of Theorem 2.8 and state the analogous result for the inner confi-*
 760 *dence sets obtained using the distance transformation.*

761 *Proof.* Consider the outer confidence sets obtained using the distance transformed scores. Then
 762 given $1 \leq i \leq n$ such that $H(\hat{M}(X_i), Y_i) \leq k$, we have

$$764 \quad 765 \quad Y_i = (Y_i \cap \hat{M}(X_i)) \cup (Y_i \cap \hat{M}(X_i)^C)$$

766 where the union is disjoint. The distance transformed scores $d_\rho(\hat{M}(X_i), v)$ are positive for $v \in$
 767 $\hat{M}(X_i)$ and negative for $v \notin \hat{M}(X_i)$. As such

$$769 \quad 770 \quad \gamma_i = \max_{v \in \mathcal{V}: Y_i(v)=1} -f_O(s(X_i), v) = \max_{v \in \mathcal{V}: Y_i(v)=1} -d_\rho(\hat{M}(X_i), v) \\ 771 \quad 772 \quad = \max_{v \in \mathcal{V}: Y_i(v)=1} \min_{e \in E(\hat{M}(X_i))} \rho(v, e) \leq H(\hat{M}(X_i), Y_i) \leq k.$$

773 Since this holds for all i on a set J which has $\frac{|J|}{n} > 1 - \alpha_2$, it follows that $\lambda_O(\alpha_2) \leq k$. In particular,
 774 arguing similarly in the opposite direction it follows that for any new observation X_{n+1} we have that
 775

$$776 \quad d_H(\hat{M}(X_{n+1}), O(X_{n+1})) \leq k.$$

□

779 A similar result can be established for the inner confidence sets via an analogous proof. We state
 780 this formally as follows.

781 **Theorem A.4.** *For each $v \in \mathcal{V}$, let $f_I(s(X), v) = d_\rho(\hat{M}(X), v)$ and define $I(X)$ as in Section 2.2.
 782 Suppose that $H(\hat{M}(X_i), Y_i) \leq k$, some $k \in \mathbb{R}$, for all $i \in J$, for some $J \subseteq \{1, \dots, n\}$ such that
 783 $\frac{|J|}{n} > 1 - \alpha_1$. Then $H(\hat{M}(X_{n+1}), I(X_{n+1})) \leq k$. In particular if $H(\hat{M}(X_{n+1}), Y_{n+1}) \leq k$, then
 784 $H(I(X_{n+1}), Y_{n+1}) \leq 2k$.*

786 A.4 DERIVING CONFIDENCE SETS FROM BOUNDING BOXES

789 We can use our results in order to provide valid inference for bounding boxes via an adaption of the
 790 approach of Andéol et al. (2023). In particular given $Z \in \mathcal{Y}$, let $B_{I,\max}(Z)$ be the largest box which
 791 can be contained within the set $\{v \in \mathcal{V} : Z(v) = 1\}$ and let $B_{O,\min}(Z)$ be the smallest box which
 792 contains the set $\{v \in \mathcal{V} : Z(v) = 1\}$. Given $Y \in \mathcal{Y}$, let $cc(Y) \subseteq \mathcal{P}(\mathcal{V})$ denote the set of connected
 793 components of the set $\{v \in \mathcal{V} : Y(v) = 1\}$ for a given connectivity criterion (which we take to be
 794 4 in our examples), and note that these components can themselves be identified as elements of \mathcal{Y} .
 795 Define

$$B_I(Y) = \bigcup_{c \in cc(Y)} B_{I,\max}(c) \text{ and } B_O(Y) = \bigcup_{c \in cc(Y)} B_{O,\min}(c)$$

796 to be the unions of the largest inner and smallest outer boxes of the connected components of the
 797 image Y , respectively. Then define

$$799 \quad \hat{B}_I(s(X)) = \bigcup_{c \in cc(\hat{M}(X))} B_{I,\max}(c) \text{ and } \hat{B}_O(s(X)) = \bigcup_{c \in cc(\hat{M}(X))} B_{O,\min}(c)$$

800 to be the unions of the largest inner and smallest outer boxes of the connected components of the
 801 predicted mask $\hat{M}(X)$, respectively. Note that this is well-defined as $\hat{M}(X)$ is a function of $s(X)$.

802 For the remainder of this section we shall assume that $\mathcal{V} \subset \mathbb{R}^2$, this is not strictly necessary but
 803 will help to simplify notation. Given $u, v \in \mathcal{V}$, write $u = (u_1, u_2)$ and $v = (v_1, v_2)$ and let
 804 $\rho(u, v) = \max(|u_1 - v_1|, |u_2 - v_2|)$ be the chessboard metric.

805 **Definition A.5.** (Bounding box scores) For each $X \in \mathcal{X}$ and $v \in \mathcal{V}$, let

$$807 \quad 808 \quad b_I(s(X), v) = d_\rho(\hat{B}_I(s(X)), v) \text{ and } b_O(s(X), v) = d_\rho(\hat{B}_O(s(X)), v)$$

809 be the distance transformed scores based on the chessboard distance to the predicted inner and outer
 810 box collections $\hat{B}_I(s(X))$ and $\hat{B}_O(s(X))$, respectively. We also define a combination of these b_M ,

primarily for the purposes of plotting in Figure 2, as follows. Let $b_M(s(X), v) = b_O(s(X), v)$ for each $v \notin \hat{B}_O(s(X))$ and let $b_M(s(X), v) = \max(b_I(s(X), v), 0)$ for $v \in \hat{B}_O(s(X))$. We shall write $b_I(s(X)) \in \mathcal{X}$ to denote the image which has $b_I(s(X))(v) = b_I(s(X), v)$ and similarly for $b_O(s(X))$ and $b_M(s(X))$.

Now consider the sequences of image pairs $(X_i, B_i^I)_{i=1}^n$ and $(X_i, B_i^O)_{i=1}^n$. These both satisfy exchangeability and so, applying Theorems A.2 and A.3, we obtain the following bounding box validity results.

Corollary A.6. (Marginal inner bounding boxes) Suppose Assumption 1 holds and that $(X_i, Y_i)_{i=1}^{n+1}$ is independent of the functions s and b_I . Given $\alpha_1 \in (0, 1)$, define

$$\lambda_I(\alpha_1) = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n 1 [C(B_i^I, b_I(s(X_i))) \leq \lambda] \geq \frac{\lceil (1 - \alpha_1)(n + 1) \rceil}{n} \right\}, \quad (10)$$

for a suitable combination function C , and define $I(X) = \{v \in \mathcal{V} : C(v, b_I(s(X))) > \lambda_I(\alpha_1)\}$. Then,

$$\mathbb{P}(I(X_{n+1}) \subseteq B_{n+1}^I \subseteq \{v \in \mathcal{V} : Y_{n+1}(v) = 1\}) \geq 1 - \alpha_1.$$

Corollary A.7. (Marginal outer bounding boxes) Suppose Assumption 1 holds and that $(X_i, Y_i)_{i=1}^{n+1}$ is independent of the functions s and b_O . Given $\alpha_2 \in (0, 1)$, define

$$\lambda_O(\alpha_2) = \inf \left\{ \lambda : \frac{1}{n} \sum_{i=1}^n 1 [C(B_i^O, -b_O(s(X_i))) \leq \lambda] \geq \frac{\lceil (1 - \alpha_2)(n + 1) \rceil}{n} \right\}. \quad (11)$$

for a suitable combination function C , and let $O(X) = \{v \in \mathcal{V} : C(v, -b_O(s(X))) \leq \lambda_O(\alpha_2)\}$. Then,

$$\mathbb{P}(\{v \in \mathcal{V} : Y_{n+1}(v) = 1\} \subseteq B_{n+1}^O \subseteq O(X_{n+1})) \geq 1 - \alpha_2.$$

Joint results can be obtained in a similar manner to those in Section 2.3.

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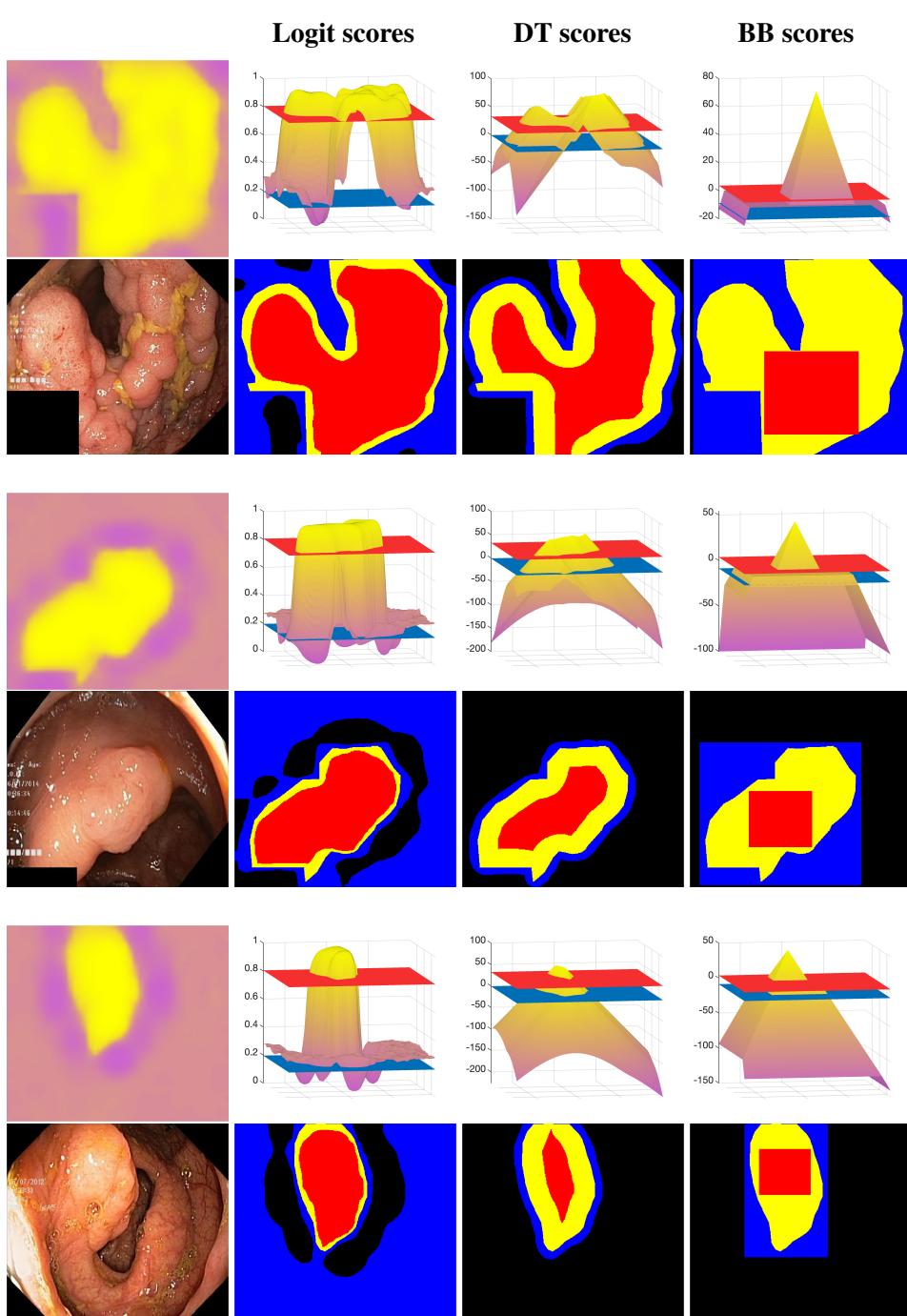
A.5 ADDITIONAL SETTINGS FOR POLYPS SEGMENTATION

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Here we plot additional settings and examples for the polyps data application. The version of the method which uses the distance transformation to create outer confidence sets and the untransformed logit scores to create inner confidence sets will be referred to as combo.

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A.5.1 ADDITIONAL EXAMPLES FROM THE LEARNING DATASET

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A.5.1 ADDITIONAL EXAMPLES FROM THE LEARNING DATASET

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Logit scores DT scores BB scores

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Here we plot additional settings and examples for the polyps data application. The version of the method which uses the distance transformation to create outer confidence sets and the untransformed logit scores to create inner confidence sets will be referred to as combo.

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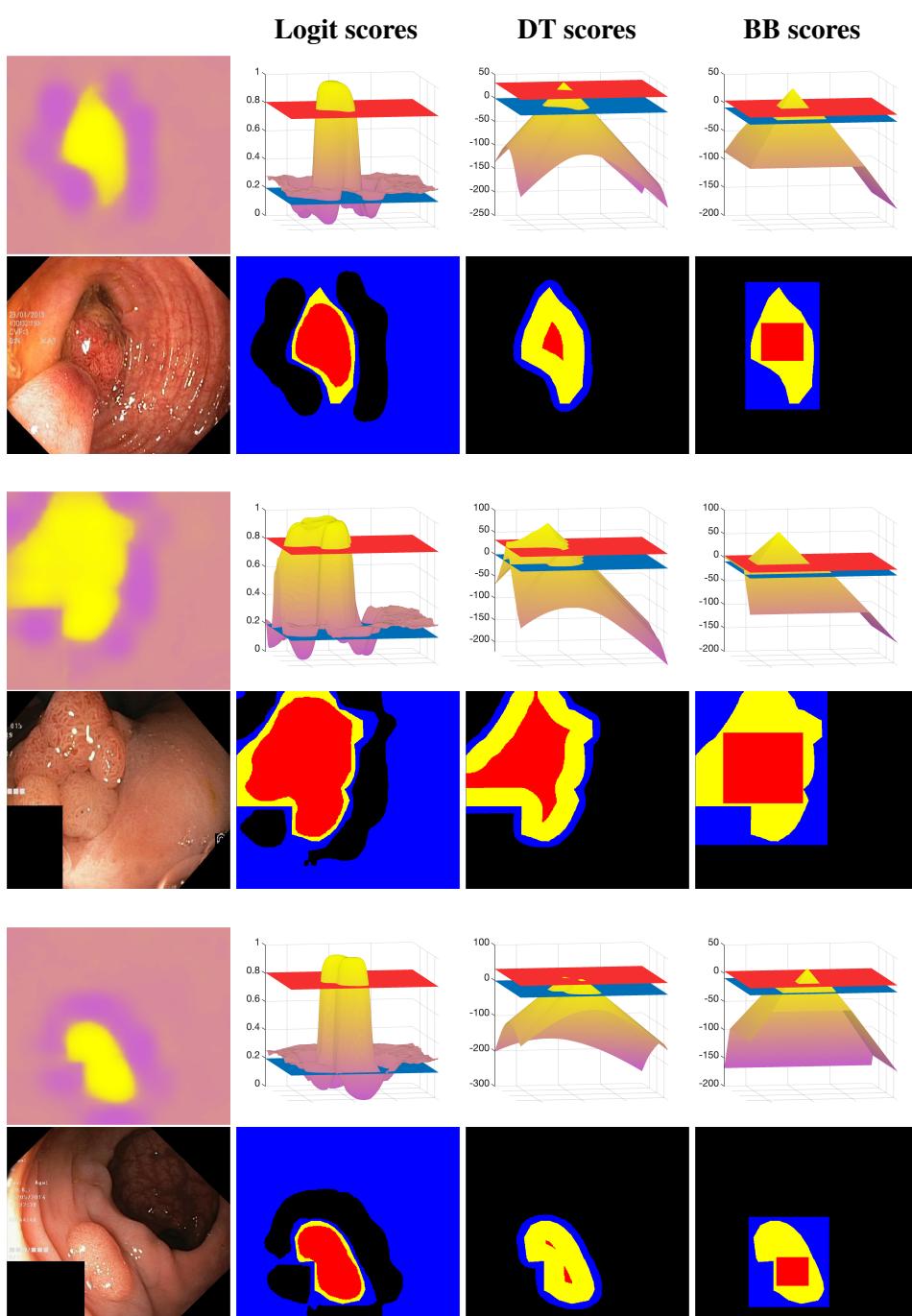
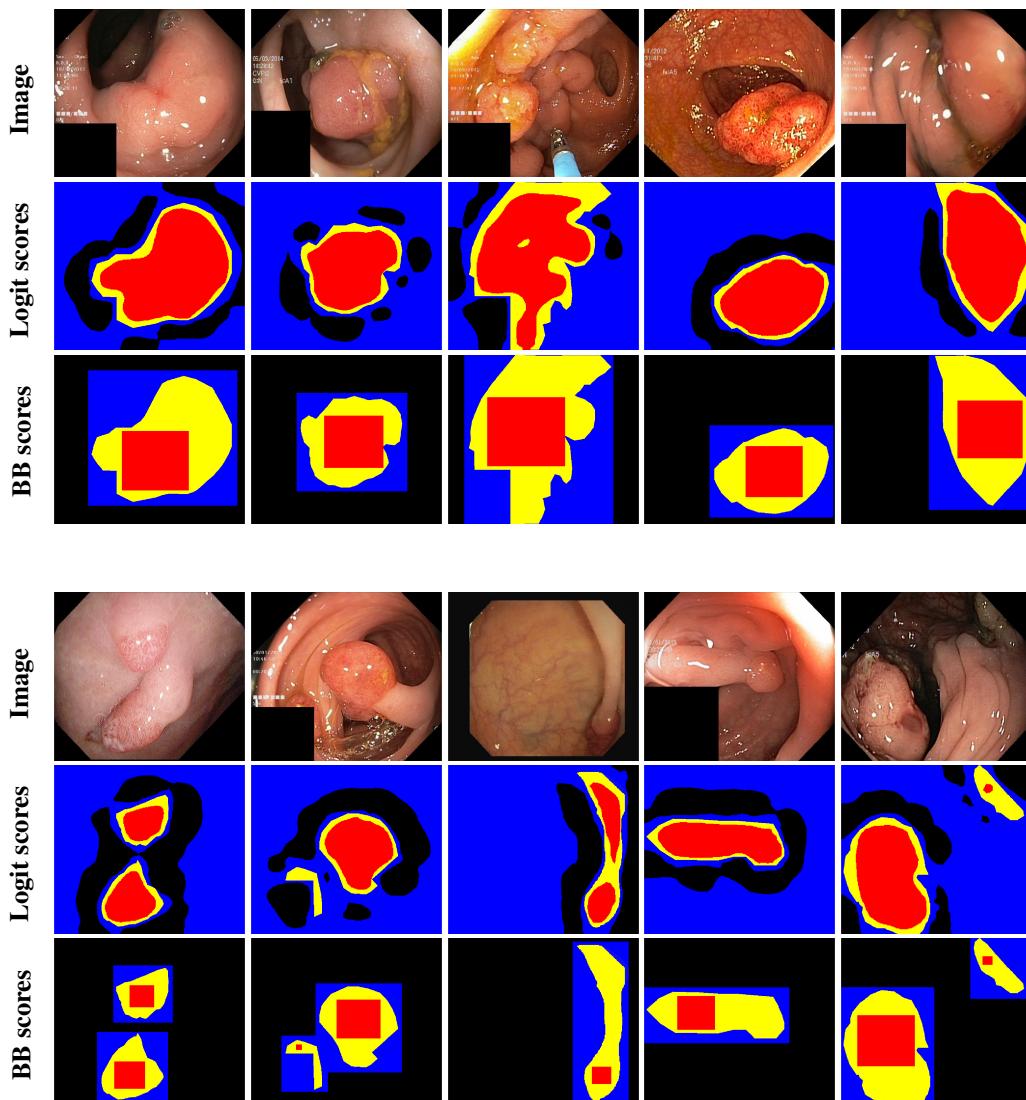


Figure A9: Futher examples from the learning dataset. The layout of these figures is the same as for Figure 2.

972 A.5.2 VALIDATION FIGURES FOR THE ORIGINAL AND BOUNDING BOX SCORES
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1010 Figure A10: Conformal confidence sets for the polyps data examples from Figure 3 for alternative
1011 scores. In each set of panels the confidence obtained from using the logit scores are shown in the
1012 middle row and those obtained from the bounding box scores are shown in the bottom row. As
1013 observed on the learning dataset the outer sets obtained when using the logit scores are very large
1014 and uninformative.

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A.5.3 ADDITIONAL VALIDATION FIGURES

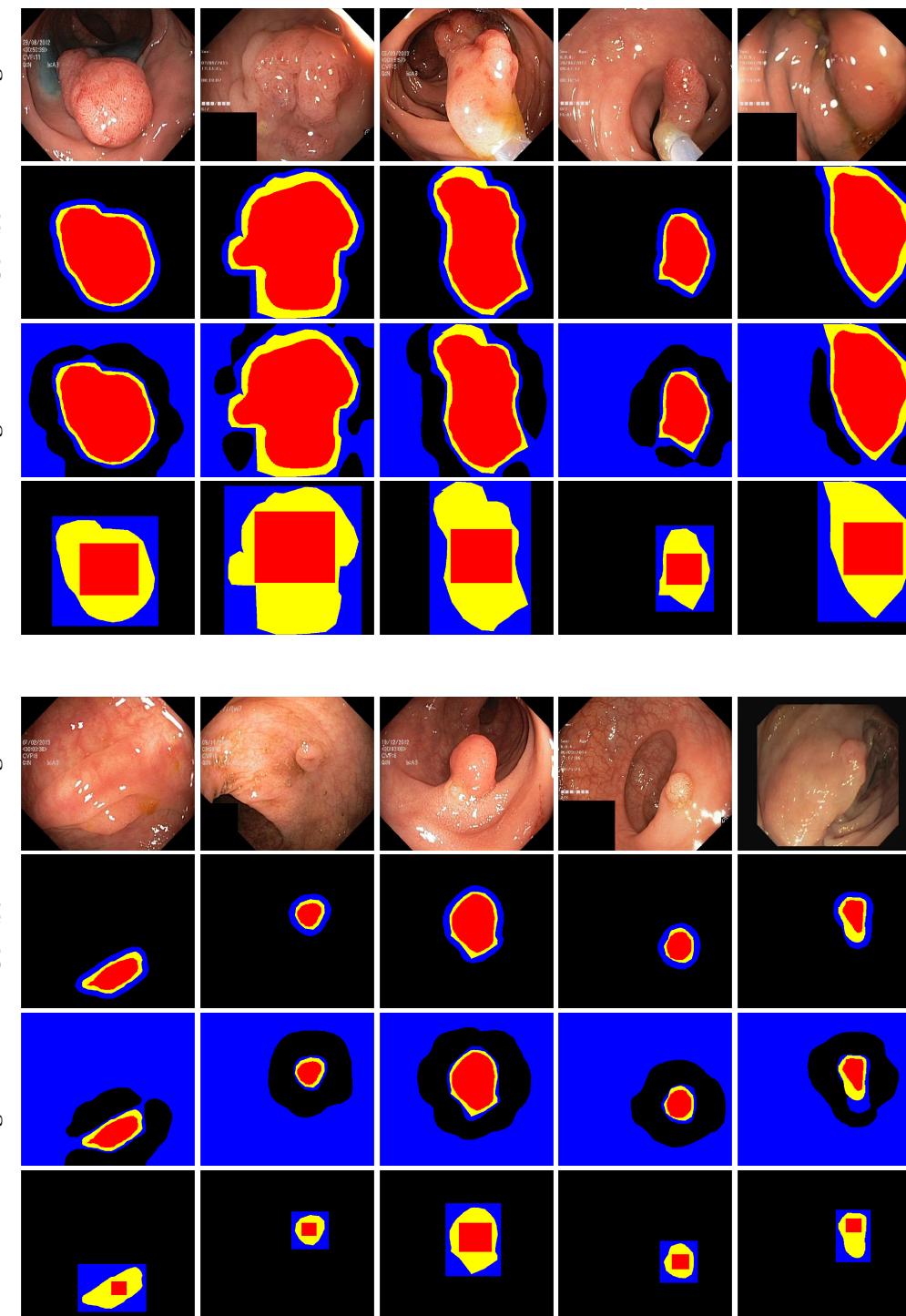
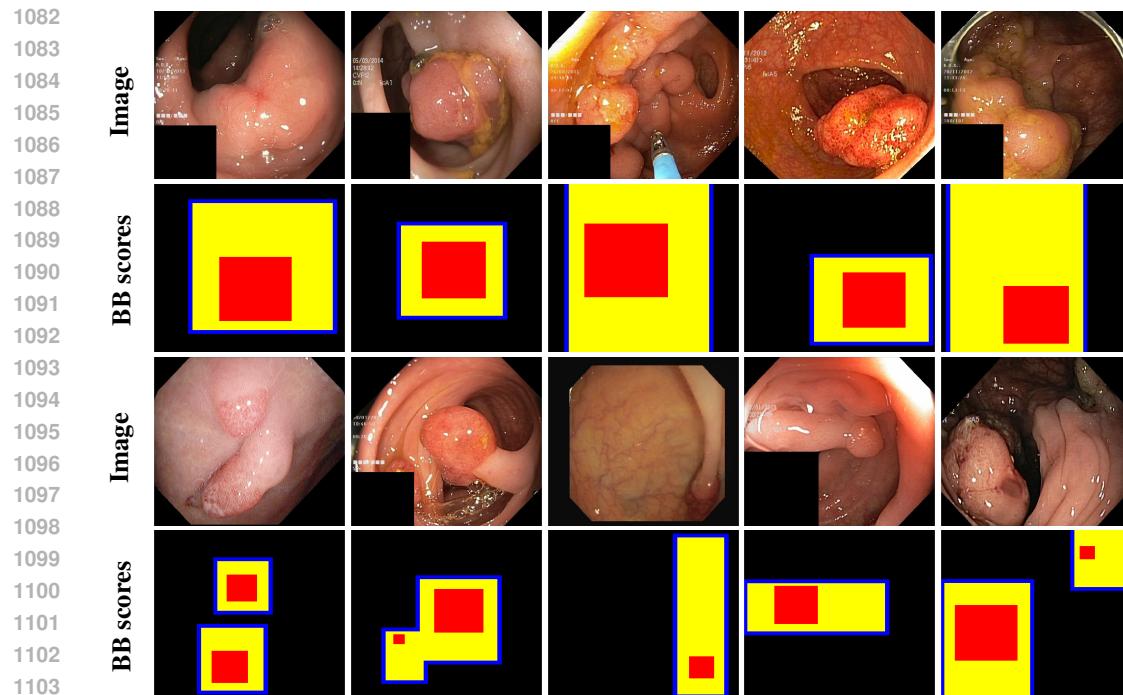


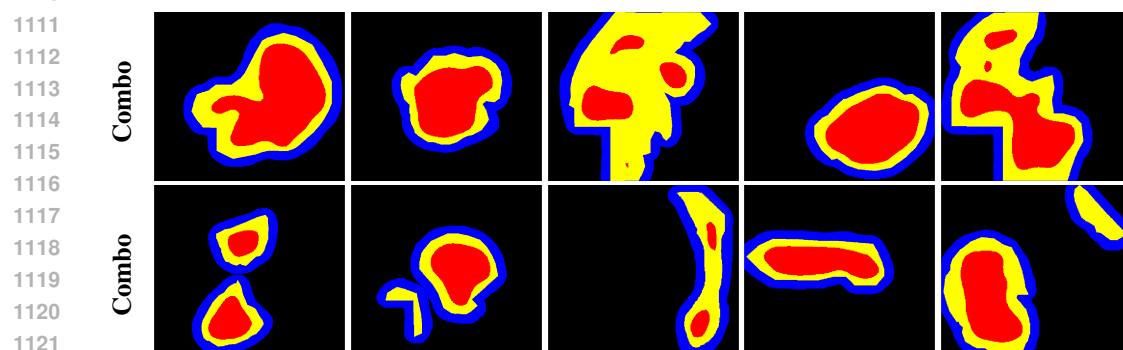
Figure A11: Additional validation examples. In each example, after the original images, the rows are (from top to bottom) the combination of the original and distance transformed scores, then the logit scores and finally the bounding box scores. The interpretation of the results is the same as for Figure 3.

1080 A.5.4 CONFIDENCE SETS FOR THE BOUNDING BOXES
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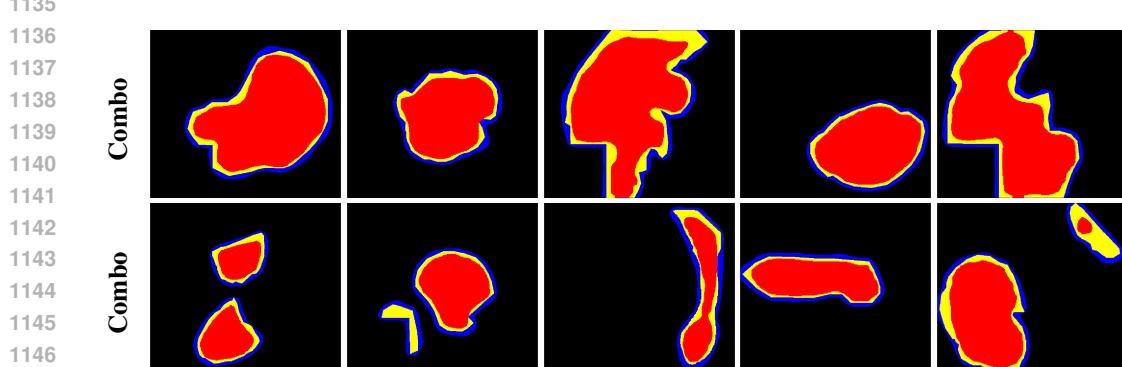


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 1105 Figure A12: Conformal confidence sets for the boundary boxes themselves using the approach
 1106 introduced in Section A.4. The ground truth outer bounding boxes are shown in yellow.
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1108 A.5.5 JOINT 90% CONFIDENCE REGIONS
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 1112 Figure A13: Joint 90% conformal confidence sets obtained using Corollary 2.5, with $\alpha_1 = 0.02$ and
 1113 $\alpha_2 = 0.08$, for the polyps images in Figure 3.
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1134 A.5.6 MARGINAL 80 % CONFIDENCE REGIONS
11351146 Figure A14: Marginal 80% conformal confidence sets obtained for the polyps images in Figure 3.
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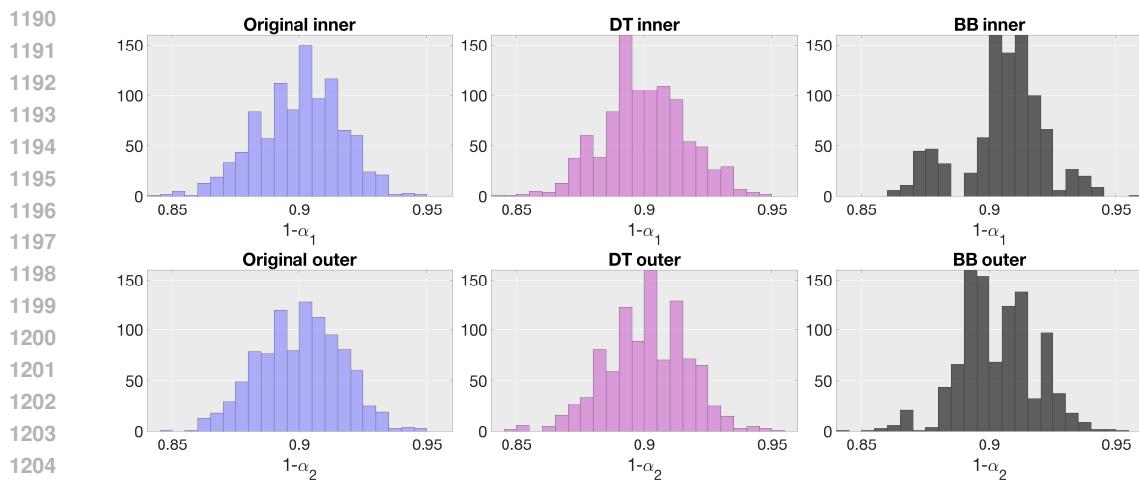
1148 A.5.7 MARGINAL 95 % CONFIDENCE REGIONS
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Figure A15 consists of a 2x5 grid of heatmaps. The rows are labeled 'Combo' on the left. The columns represent five different polyp images, each showing a blue heatmap indicating the 95% marginal conformal confidence set against a black background.

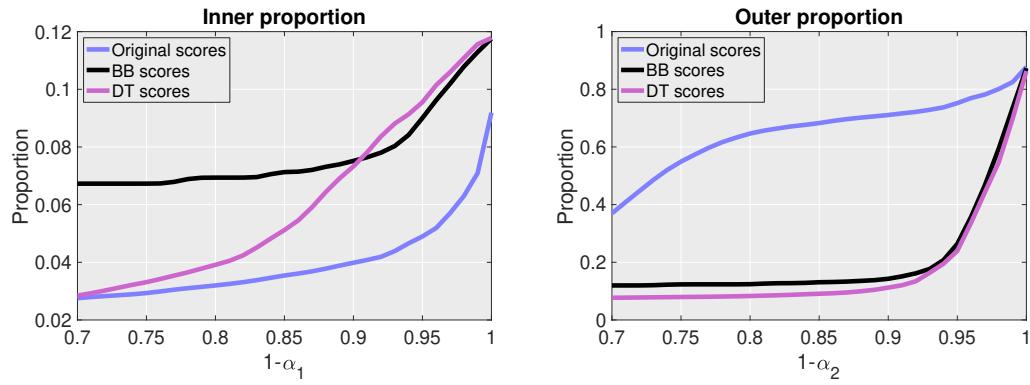
1150 Figure A15: Marginal 95% conformal confidence sets obtained using for the polyps images in Figure
1151 3. These sets are also joint 90% confidence sets with equally weighted $\alpha_1 = \alpha_2 = 0.05$. The
1152 influence of the weighting scheme can therefore examined by comparing to Figure A13.
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1188 A.5.8 HISTOGRAMS OF THE COVERAGE
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1206 Figure A16: Histograms of the coverage rates obtained across each of the validation resamples for
1207 90% inner and outer marginal confidence sets. We plot the results for the logit scores, distance
1208 transformed scores (DT) and boundary box scores (BB) from left to right. The bounding box scores
1209 are discontinuous which is the cause of the discreteness of the rightmost histograms.

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1211 A.5.9 COMPARING THE PROPORTION
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1226 Figure A17: Measuring the proportion of the entire image which is under/over covered by the
1227 respective confidence sets. Left: proportion of the image which lies within the true mask but outside
1228 of the inner set. Right: proportion of the image which lies within the confidence set but outside of
1229 the true mask. For both a lower proportion corresponds to increased precision.

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A.6 ADDITIONAL SETTINGS FOR BRAIN MASK SEGMENTATION

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1245A.6.1 COMPARING ORIGINAL AND DISTANCE TRANSFORMED SCORES ON THE LEARNING
1246 DATASET

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Figure A18: *Learning the best transformation for brain mask segmentation. First row: original images from different subjects. Second row: confidence sets provided by calibrating the distance transformed scores on the learning dataset. Third row: confidence sets produced using the logit scores on the learning dataset. Using the logit scores produced very bad results. Instead the distance transformation is a big improvement. Note that the improvement obtained by using the distance scores is even more when using the full calibration data, see Figure 6. This is because the learning dataset is relatively small and does not capture the full picture. The results at test time for the logit scores are equally bad as for the learning data, see Figure A20.*

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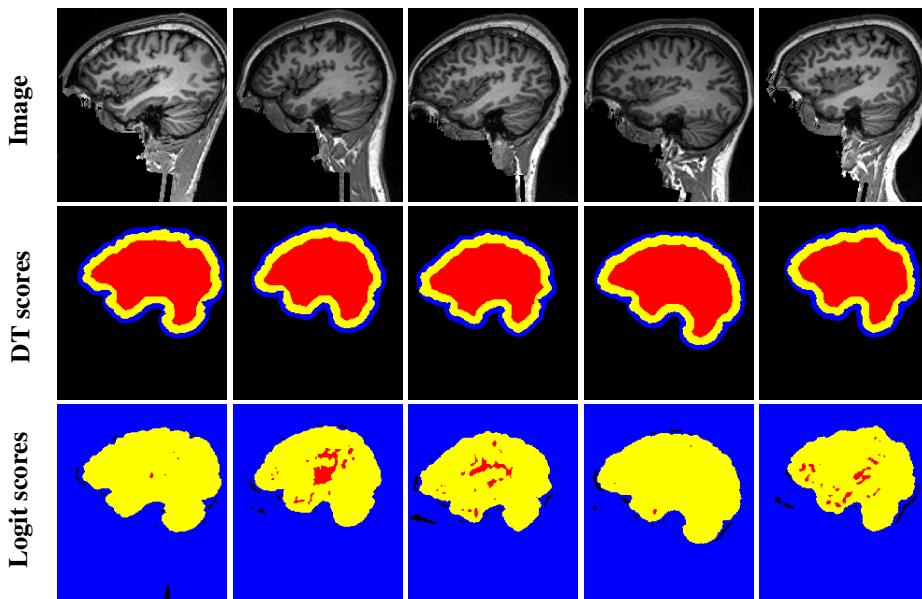
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A.6.2 COMPARING SMOOTH TRANSFORMED SCORES ON THE LEARNING DATASET

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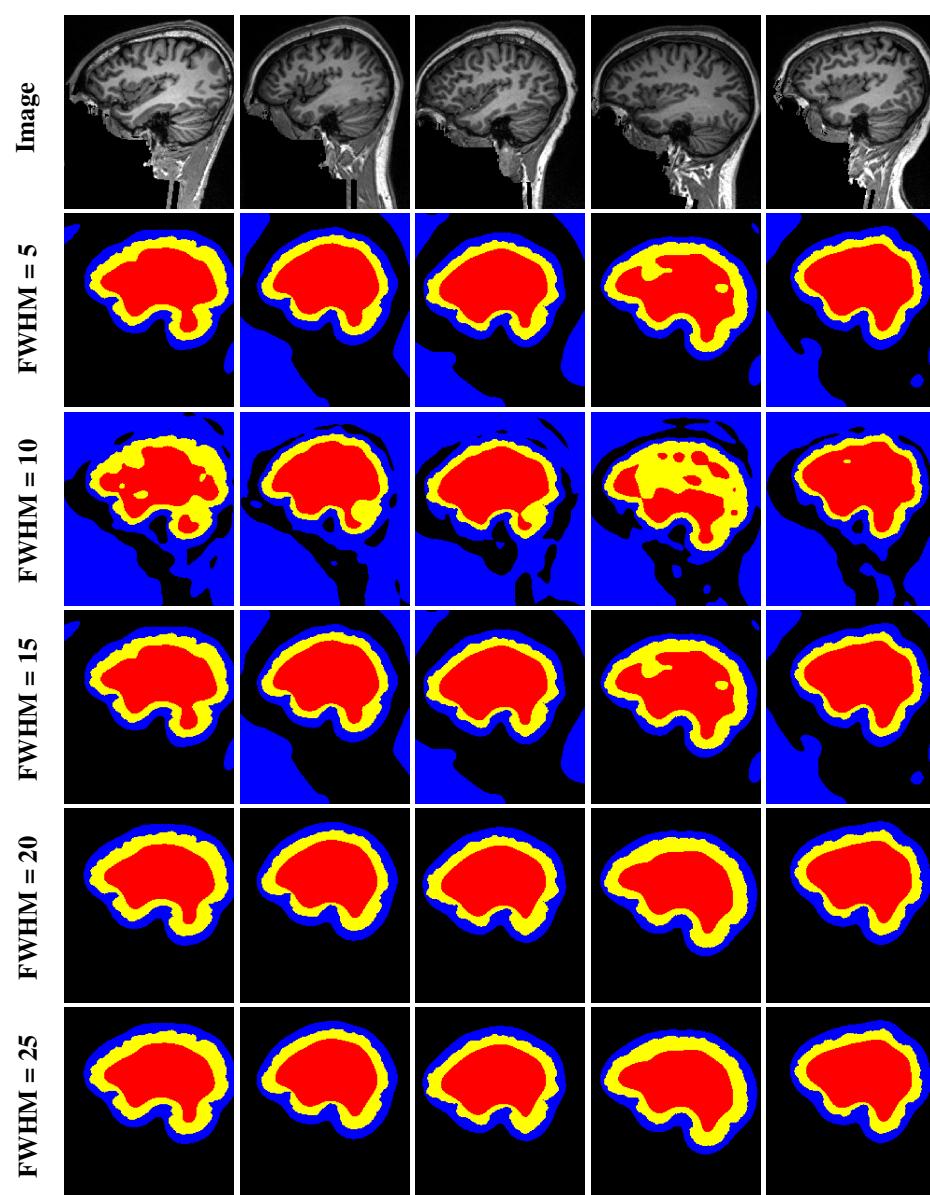


Figure A19: *Inner and outer sets computed by comparing smooth score transformations on the learning dataset. Scores were smoothed using a Gaussian kernel with full width at half maximum (FWHM) taking values in $\{5, 10, 15, 20, 25\}$ mm. The resulting inner and outer sets based on increasing levels of applied smoothness are shown from top to bottom. The performance appears to peak at 20mm.*

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A.6.3 COMPARING ORIGINAL AND DISTANCE TRANSFORMED SCORES ON THE TEST
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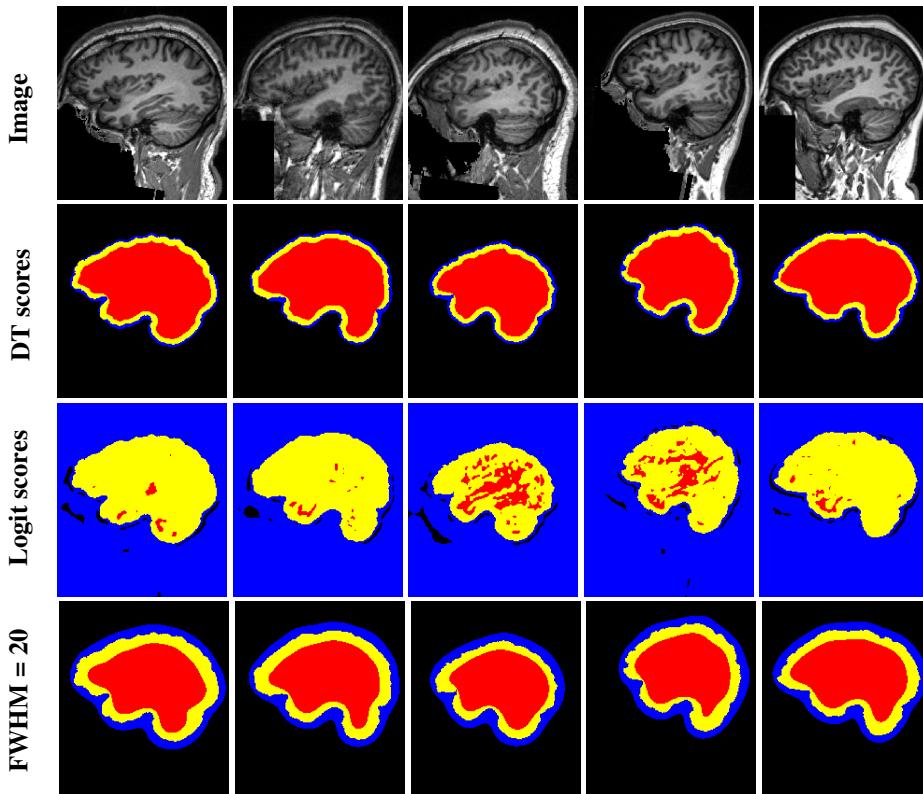


Figure A20: *Inner and outer confidence sets for brain mask segmentation using the distance transformed and logit scores. Top row: brain images for each subject. 2nd row: the inner and outer confidence sets produced by calibrating the distance transformed scores on the calibration dataset. 3rd row: the inner and outer confidence sets produced by calibrating the logit scores on the calibration dataset. 4th row: the inner and outer confidence sets produced by calibrating the smoothed scores (smoothed with an isotropic Gaussian kernel of 20mm - chosen because it performed the best on the learning dataset). As for the learning dataset the logit scores perform very poorly and are not able to separate the background from the segmented masks with confidence. Instead the distance transformed scores do a very good job at segmenting the mask. Indeed they do slightly better on the calibrated dataset than on the learning dataset. The smooth scores improve on the logit scores but do not provide as tight bounds as the distance transformed scores for neither inner nor outer sets.*

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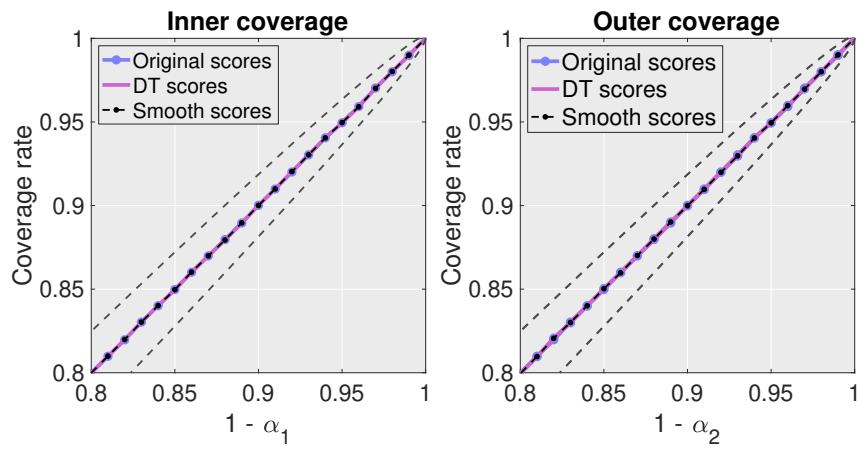
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1404 A.6.4 COMPUTING THE COVERAGE FOR THE BRAIN IMAGING DATA
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1406 In order to study the coverage rate of the methods in the context of the brain imaging application we
 1407 perform a similar validation to that described in Section 3.3 for polyps segmentation. To do so we
 1408 divide the 474 subjects left, after excluding the learning dataset, into 300 calibration and 174 test
 1409 images. We do this 1000 times, randomly sampling the sets of 300 and 174 images respectively and
 1410 measuring the coverage in each run. We average the coverage over the 1000 runs and display the
 1411 results in Figure A21. Note that unlike the box scores considered in Section 3.3, the smooth scores
 1412 are not discrete so do not display discreteness issues at lower levels of coverage.



1428 Figure A21: *Coverage levels of the inner and outer sets averaged over 1000 validations for the origi-*
 1429 *nal, distance transformed (DT) and smoothed scores (smoothed with a full width at half maximum*
 1430 *of 20mm). The nominal rate is achieved in all settings considered.*

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A.7 ADDITIONAL SETTINGS FOR TEETH SEGMENTATION

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1461A.7.1 COMPARING ORIGINAL AND DISTANCE TRANSFORMED SCORES ON THE LEARNING
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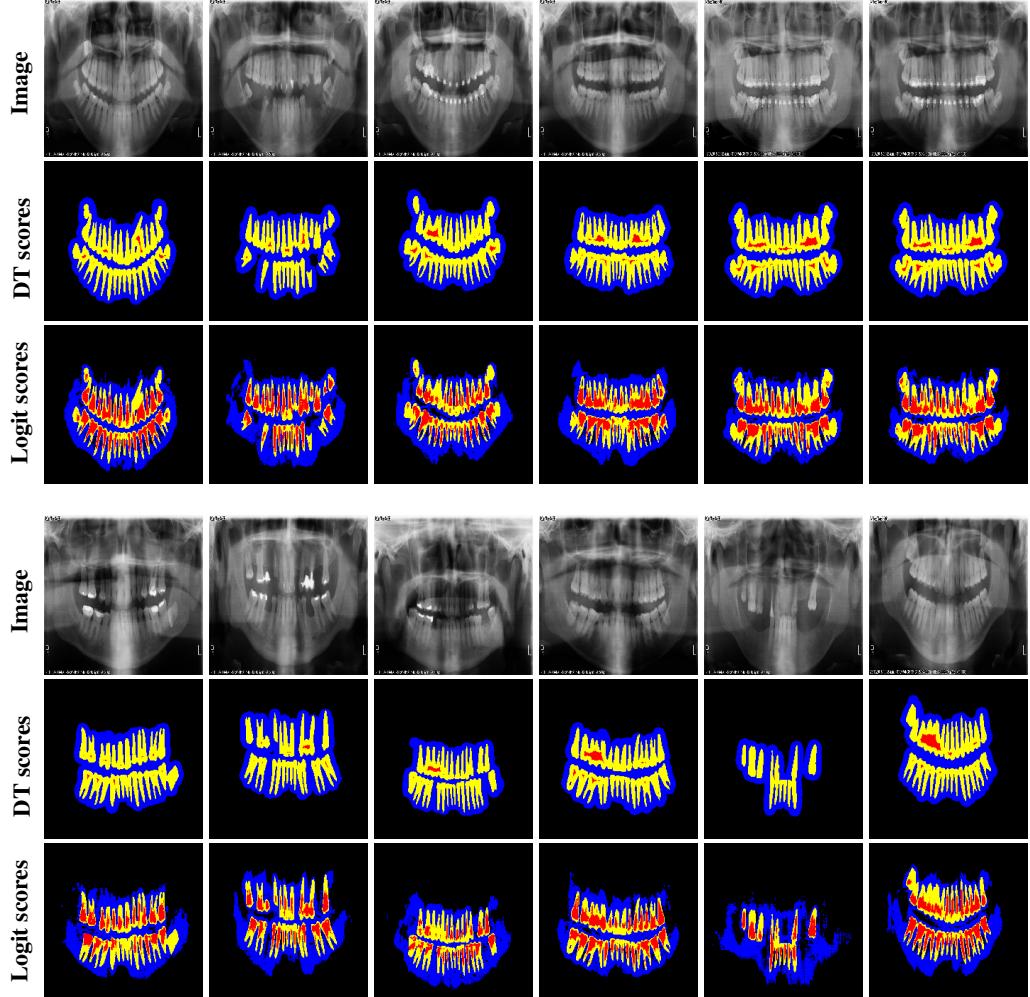
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Figure A22: *Inner and outer confidence sets for brain mask segmentation calibrated and plotted on the learning dataset.* 12 images are plotted in two sets of 6, for each set the rows are as follows. First row: original images. Second row: results of distance transformed scores - providing tight outer sets but uninformative inner sets. Third row: logit scores providing looser outer sets but more informative inner sets though these can be improved by smoothing see Figure A23.

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A.7.2 COMPARING SMOOTH TRANSFORMED SCORES ON THE LEARNING DATASET

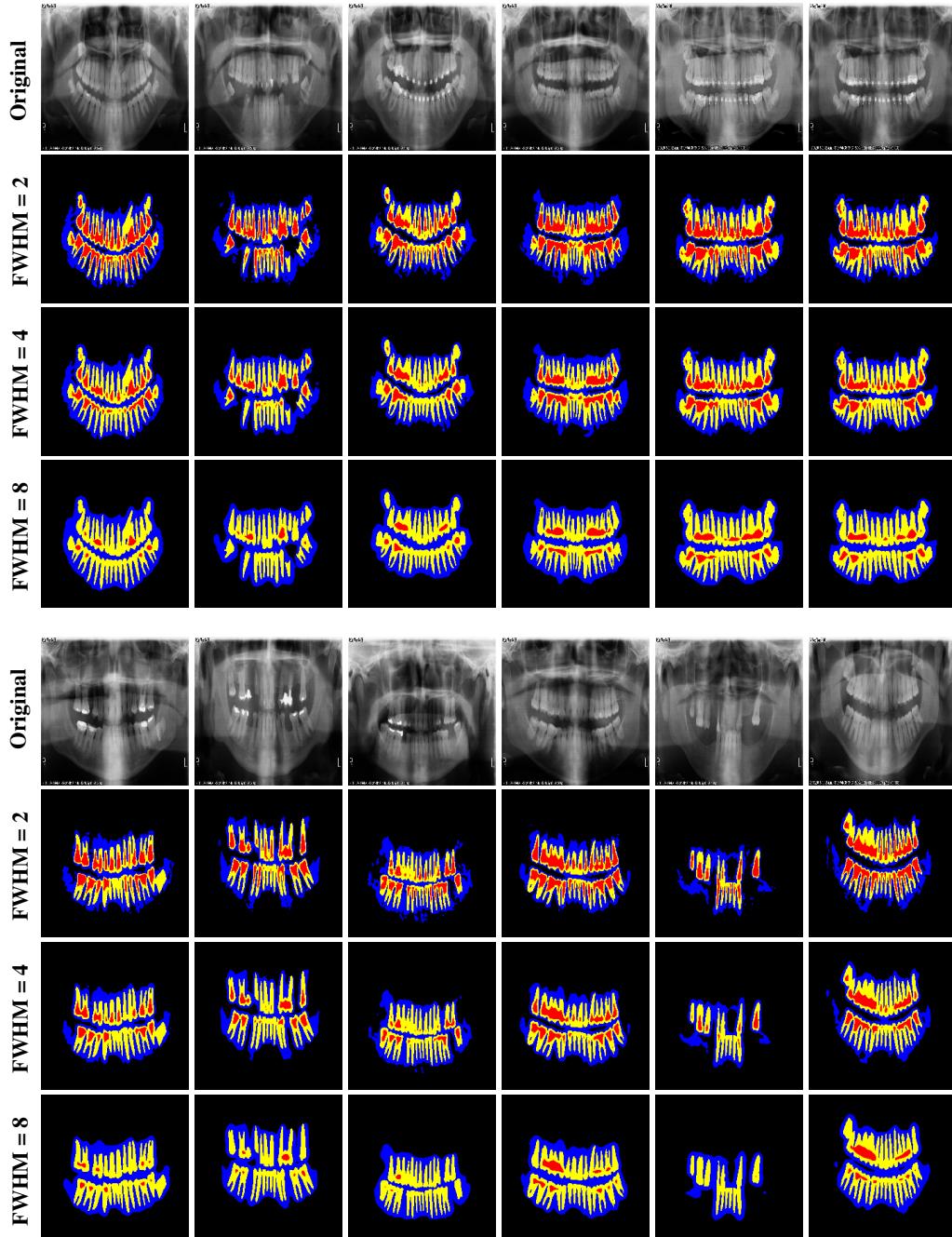
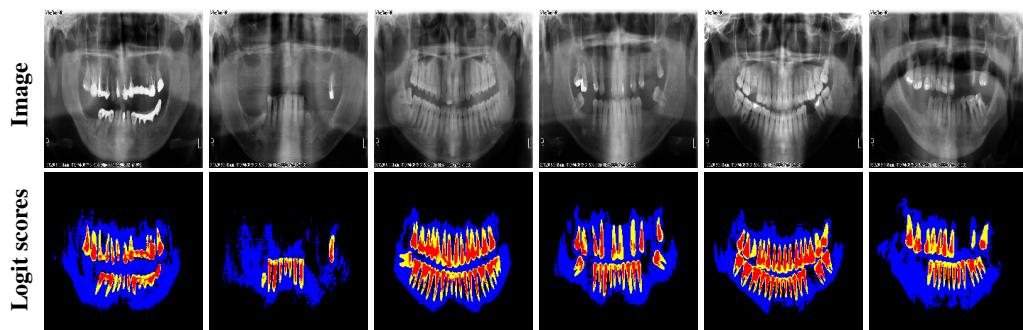


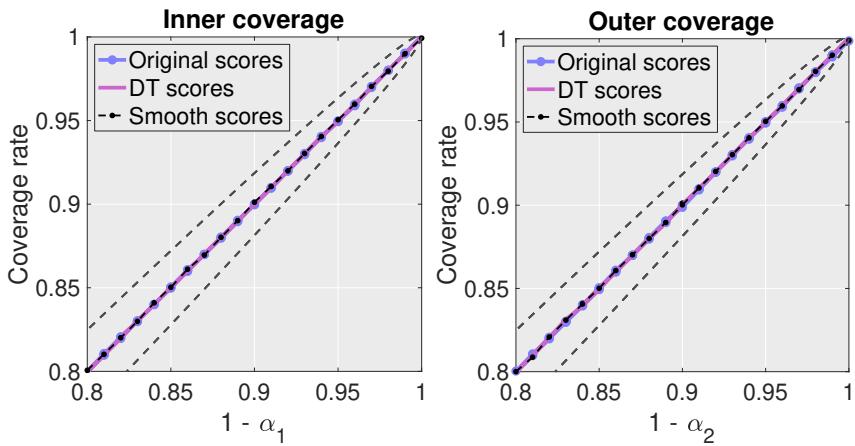
Figure A23: *Inner and outer sets computed by comparing smooth score transformations on the learning dataset. Scores were smoothed using a Gaussian kernel with full width at half maximum (FWHM) taking values in $\{2, 4, 8\}$. For each set of 6 the resulting inner and outer sets based on increasing levels of applied smoothness are shown from top to bottom. A FWHM of 2 pixels is the best for the inner set and indeed performs better than the logit scores shown in Figure A22. Instead an increased level of smoothness is better for the outer set, attaining comparable performance to the distance transformed scores though with some additional blobs.*

1566 A.7.3 COMPARING TO THE LOGIT SCORES ON THE TEST DATASET
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Figure A24: *Inner and outer confidence sets for brain mask segmentation computed using the logit scores. The performance is less good than the score transformations optimized on the learning dataset and shown in the main text but have been included for reference. The outer sets are larger and less precise than those based on the distance transformation. The inner sets are good but not quite as good as the ones based on a small amount of smoothing.*

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1586 A.7.4 COMPUTING THE COVERAGE FOR THE TEETH DATASET
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1588 In order to study the coverage rate of the methods in the context of the brain imaging application we
1589 perform a similar validation to that described in Sections 3.3 and A.6.4. To do so we divide the 198
1590 subjects, into subsets of size 170 and 28. We do this 1000 times, randomly sampling the sets of 170
1591 and 28 images respectively and measuring the coverage in each run. We average the coverage over
1592 the 1000 runs and display the results in Figure A25.



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Figure A25: *Coverage levels of the inner and outer sets averaged over 1000 validations for the original, distance transformed (DT) and smoothed scores (smoothed with a full width at half maximum of 2 pixels). The nominal rate is achieved in all settings considered.*

1620 A.8 COMPARING PERFORMANCE METRICS FOR EACH SEGMENTATION MODEL
16211622 *In the table we display performance metrics for each model, computed over the validation set used
1623 in each data application.*

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1626 Table 1: *Performance Metrics over the validation set*

Model	Application	Average Dice Score	Average Precision	Average Recall
PraNet	Polyps	0.9357	0.9365	0.9200
HDBET	Brain imaging	0.97578	0.96058	0.99158
U-Net based GAN	Teeth	0.93347	0.93548	0.93236

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A.9 RELATIONSHIP WITH MULTIPLE TESTING ERROR RATES

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FAMILY-WISE ERROR RATE (FWER)

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In traditional multiple hypothesis testing Family-Wise Error Rate (FWER) is the probability of making at least one false discovery across a set of considered hypotheses. Given a multiple testing problem in which m hypotheses are tested and a multiple testing algorithm \mathcal{M} , let $V(\mathcal{M})$ denotes the resulting set of false discoveries, $R(\mathcal{M})$ the set of rejected hypotheses and T be the set of true rejections. Then the FWER is defined as:

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$$FWER(\mathcal{M}) := \mathbb{P}(|V(\mathcal{M})| \geq 1).$$

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Then, given $\alpha > 0$, if we can guarantee that $FWER \leq \alpha$ then it follows that $R(\mathcal{M}) \subseteq T$ with probability at least $1 - \alpha$. This statement is thus analogous to the coverage guarantees which we provide in Theorems 2.1 and 2.2 in the sense that a probabilistic gaurantee on the inclusion probability is provided.

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