

Iowa Initiative for Artificial Intelligence

Final Report

Project title:	Prediction of pelvic mass malignancy on CT scan using AI
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Date:	Dec 2021
Were specific aims fulfilled:	Yes
Readiness for extramural proposal?	Yes
If yes ... Planned submission date	A preliminary proposal was submitted on June 14, 2021. A full grant proposal was invited to submit on September 15, 2021.
Funding agency	Ovarian Cancer Research Alliance
Grant mechanism	External, non-federal
If no ... Why not? What went wrong?	

Brief summary of accomplished results:

We developed a convolutional neural network model for predicting surgical outcomes in ovarian cancer (OC). Our deep learning prediction model was based on a VGG network, which consisted of nine convolution layers with 3×3 kernel size for each layer of convolution. The novelty resides in the use of additional input channel of segmentation masks, which introduces an attention mechanism for the prediction model to focus on learning prominent image features centered at the tumor. With a five-fold validation on 178 OC cases treated with surgery at the University of Iowa, our prediction model achieved an accuracy of 78%, which outperformed the model without using segmentation masks as an input channel whose prediction accuracy was 75%.

Research report:

Aims (provided by PI):

Ovarian cancer is a leading cause of cancer death among women in the United States, partly because most patients present with advanced disease at diagnosis.¹ The initial treatment consists of the combination of primary cytoreductive surgery (PCS) and chemotherapy.² PCS is considered successful (or '*optimal*') when the diameter of any residual disease after surgery is <1 cm, based on recent practice guidelines from the Society of Gynecologic Oncology (SGO) and the American Society of Clinical Oncology (ASCO).^{3,4} But PCS can only be achieved in a portion of patients,⁵ and every gynecologic oncologist is faced with a dilemma when making the diagnosis of ovarian

cancer: Do I take this patient to surgery immediately achieving optimal PCS upfront, or should this patient receive neoadjuvant chemotherapy prior to surgery because optimal PCS is unlikely or unsafe for her? The answer to this critical question is currently determined subjectively in most cases, though it is clear that those patients whose initial surgery is optimal have a major survival advantage.^{5,6} Thus, there is a critical need to better identify those individual patients who can most benefit from initial surgery versus neoadjuvant chemotherapy in order to improve outcomes for patients with high-grade serous ovarian cancer (HGSC).

Our central hypothesis is that integration of clinical, radiological and molecular data from HGSC would result on a better prediction model for optimal surgical outcomes that would have added clinical value. Leveraging the vast Biobank at the University of Iowa, we have identified of a cohort of 359 patients with advanced stage HGSC with banked tumor tissues. This UI biobank of ovarian cancer specimens is unique in the field, as we have one of the best clinical follow-up data available of any public dataset. Fresh frozen tumor was collected from 150 of these patients, RNA and DNA was extracted, and gene and miRNA expression, somatic mutations, gene copy number alterations and promoter DNA methylation have been determined in 112 of these patients. Additionally, 178 of these patients had CT imaging studies performed previously to their surgery for HGSC and their images have been processed and stored for analysis. These biologic variables, when combined with clinical and radiologic features, provide a rich source of data for modeling outcomes. Thus, our specific aims are:

Aim 1: To create and optimize prediction models for optimal surgical outcomes of HGSC patients.

Aim 2: To improve the performance of deep learning models by integrating clinical data and other imaging data.

Data:

The UI Gynecologic Oncology Biobank has a long-standing Institutional Review Board (IRB) approved protocol (IRB#200209010, Molecular and Genetic Study of Gynecologic Cancers) for specimen and outcome data collection. Also, recently the IRB approved the study dedicated to prospectively collect information from patients with suspected advanced stage HGSC (IRB#201804817). This Biobank has been collecting gynecologic cancer specimens (tumor, blood, urine) for over 25 years, with >3,000 stored specimens and de-identified patient data available for nearly all specimens.

In this project, we identified a cohort of 178 patients with advanced stage HGSC from the UI. Clinical information was abstracted from these patients. Abdominal CT scans were identified, extracted, and formatted for those patients. Furthermore, fresh frozen tumor was collected from 150 of these patients, and 112 of them had good quality RNA and DNA to proceed with RNA-seq and DNA promoter methylation. Gene and miRNA expression, somatic mutations, DNA methylation and gene copy number alteration have been determined and can be used to create prediction models of optimal surgical outcomes in conjunction with CT images processed with AI algorithms.

AI/ML Approach:

we implemented a convolutional neural network model for predicting surgical outcomes in OC. Our deep learning prediction model (Figure 1) was based on a VGG network,⁷ which consisted of nine convolution layers with 3×3 kernel size for each layer of convolution. The convolution stride was fixed to one pixel and the spatial padding for each convolution layer input was applied so that the spatial resolution was preserved after convolution. Max-pooling was performed over a 2×2 window to down-sample the feature

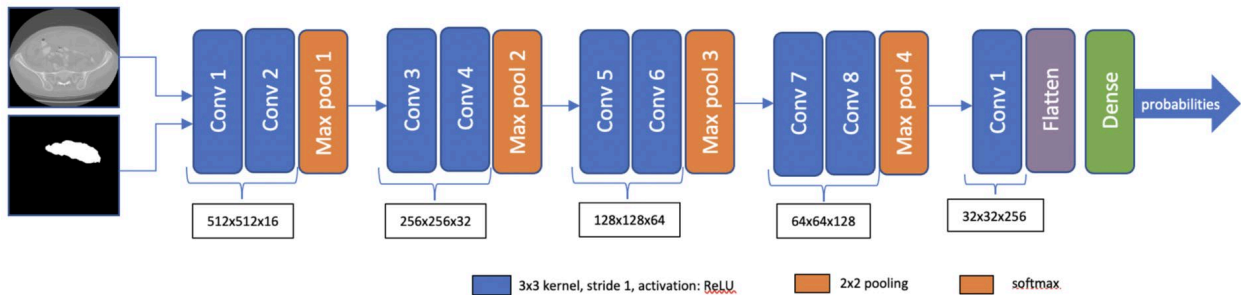


Figure 1. Deep CNN-based prognostication network for the prediction of surgical outcomes. The VGG 16 network⁷ was used as the backbone of the prediction network. The segmentation masks were used as an additional input channel.

maps by two, with a stride of one. We started with 16 feature maps in the first convolution layer, which were doubled after every two convolution layers. At the end of these convolution layers, all feature maps were flattened and a dense layer with two channels was added with a soft-max activation to predict the surgical outcomes (optimal or not). All hidden layers were equipped with non-linear rectification (ReLU).⁸ The novelty resides in the use of additional input channel of segmentation masks, which introduces an attention mechanism for the prediction model to focus on learning prominent image features centered at the tumor.

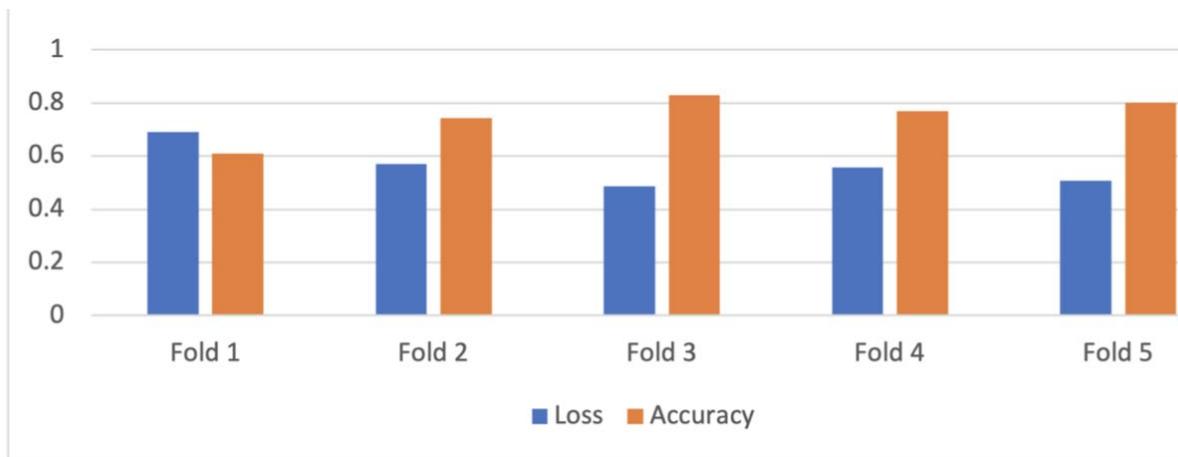


Figure 2. The loss and accuracy score on each of the five folds.

Experimental methods and results:

With a five-fold validation on 178 OC cases treated with surgery at the University of Iowa, our prediction model achieved an accuracy of 78%, which outperformed the VGG model without using segmentation masks as an input channel whose prediction accuracy was

75%. The accuracy scores on five folds are shown in Figure 2. The performance comparisons of the proposed VGG prediction model to XceptionNet and MobileNet with respect to accuracy, sensitivity, and specificity are shown in Figure 3. As an integrative part of our model validation, we attempted to unfold the “black box” nature of the proposed prediction model through deep network visualization tools. The interpretability method of Gradient-weighted Class Activation Mapping (GradCAM) ⁹ was used to unfold the activation of the network layers to produce heat map prediction of regions at risk. The heatmaps (Figure 4) demonstrated that the proposed prediction model focused on the features around anomalous OC regions.

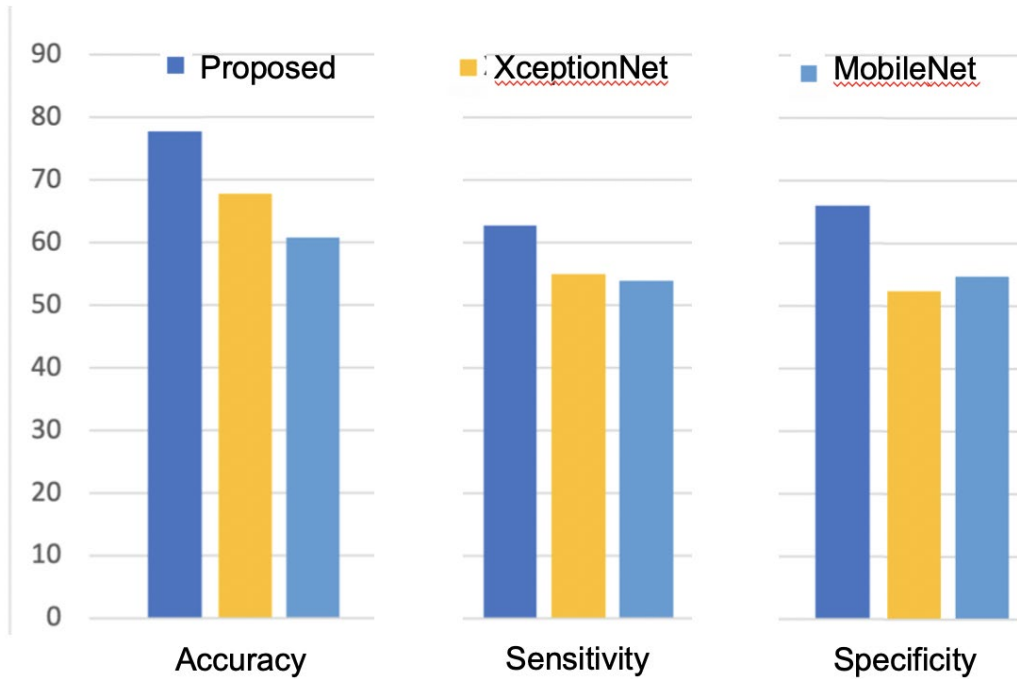


Figure 3. Performance comparisons of the proposed method to XceptionNet and MobileNet with respect to accuracy, sensitivity, and specificity.

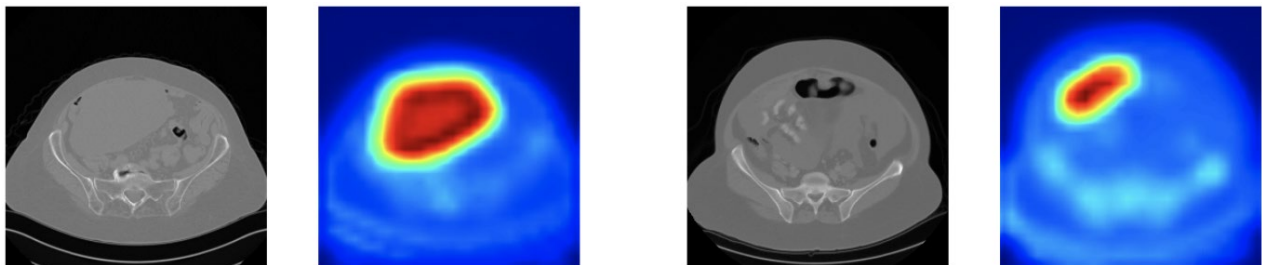


Figure 4. Example heatmaps showing essential features of the proposed prediction model.

Ideas/aims for future extramural project:

Inspired by this pilot project, we have got invited to submit a grant proposal to the Ovarian Cancer Research Alliance. We propose to adopt a two-step framework for the development of our deep learning segmentation-based predictive model using CT images with correlative clinical metadata to discriminate OC from benign pelvic masses before surgery. The proposed model is termed as a DeSep-OC model. We plan to first develop a prediction model DeSep-OC_T that only makes use of the pre-surgery CT images for the pelvic mass malignancy prediction (**Aim 1**), then we will integrate clinical data and other imaging data into the DeSep-OC_T model to fully develop the proposed DeSep-OC model (**Aim 2**). Our approach overcomes three common barriers of the current deep diagnosis models: 1) the inherent issue of overfitting caused by a large number of model parameters; 2) the necessity of incorporating supplementary hand-crafted radiomic features; and, 3) the 'black box' nature and limited interpretability.

Publications resulting from project:

N/A

References:

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