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GENERATIVE ADVERSARIAL NETWORKS IN TUMOR-RELATED RESEARCH: A REVIEW AND AGENDA FOR MOVING FORWARD

Andrew Behrens
Dakota State University, andrew.behrens@dsu.edu

Cherie Noteboom
Dakota State University, cherie.noteboom@dsu.edu

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Andrew J. Behrens
Dakota State University
Andrew.Behrens@dsu.edu

Cherie Noteboom
Dakota State University
Cherie.Noteboom@dsu.edu

ABSTRACT

Recent advances in Generative Adversarial Networks (GANs) have led to many new uses of GANs. The latest advancements have allowed researchers and practitioners to apply this them to tumor-related problems with limited data. This research investigated literature on GANs and their uses in tumor-related research. The literature surveyed utilized academic databases over the course of June 2014 and February 2021. This paper aims to develop a research agenda for information systems through a systematic literature review that investigates practitioners' and researchers' emerging issues and current works on the topic. Emerging implementation trends and limitations of GANs in tumor-related problems are also explored. The findings showed that there is a significant gap between GAN development and implementation and that there are many areas where researchers and practitioners can contribute to further the research and application of GANs.

Keywords

Generative adversarial network, tumors, healthcare, data-driven systems, decision support

INTRODUCTION

Generative Adversarial Networks (GANs) were proposed by Goodfellow et al. in 2014 (Goodfellow et al., 2014). GANs provide a way to learn deep representations without extensively annotated training data (Creswell et al., 2018). Their application and ability to synthesize and augment data stimulated their use within the medical imaging domain. GANs were considered a popular semi-supervised and unsupervised machine learning approach for medical image analysis. There are different architectures of GANs which are used as alternative approaches to problems. The various architectures are fully connected, convolutional, conditional, inference models, and adversarial autoencoders (Creswell et al., 2018).

A gap between the development of GANs and their implementation currently exists in tumor-related research. Practitioners are concerned with current challenges in their particular work settings, while academics develop more generalizable rules and understanding (Belanger et al., 2002). Academics focus more on understanding a rigorous comparison between different GANs and practitioners focus on developing high-performing GANs that solve problems. GANs are gaining popularity, therefore it is important to understand the gap between development and implementation and set forth an agenda for the information systems discipline.

Therefore, two objectives are posited in this paper:

1. To examine the gap between GAN development and implementation in tumor-related research; and
2. To identify a research agenda to address emerging issues and concerns relevant to the information systems discipline.

This study proceeds by examining the gap between GAN development and variant implementation through a systematic literature review. First, we define a specific methodology. Following that, a brief literature review is completed to summarize the current state of the literature and identify gaps. The results are presented and discussed. A brief research agenda is proposed in the discussion and identifies research gaps. The article will conclude with reflections on the findings following the agenda. The main contribution of this paper is to examine the development and implementation gap of GANs and propose an information systems research agenda for moving forward.

METHODOLOGY

Overview

This review followed the PRISMA guidelines (Liberati et al., 2009). The PRISMA chart is shown in Figure 1. Eligible articles were searched for in MEDLINE, IEEE, ScienceDirect, BSP, ACM, and ASP. The papers collected were from June 2014 and February 2021. The search strategy for each database was completed using the keywords "generative adversarial network" and "tumor." Original research studies were included that used GANs for tumor-related research.

The excluded studies did not match the keyword in the title or abstract. Since GANs were developed in 2014, studies before then were excluded. Inclusion eligibility was assessed individually by evaluating the title and abstract of the article for the keywords suggested above in the search strategy. The included studies that met the search strategy were classified through Table 1. The same researcher evaluated and classified the full text of the included articles.

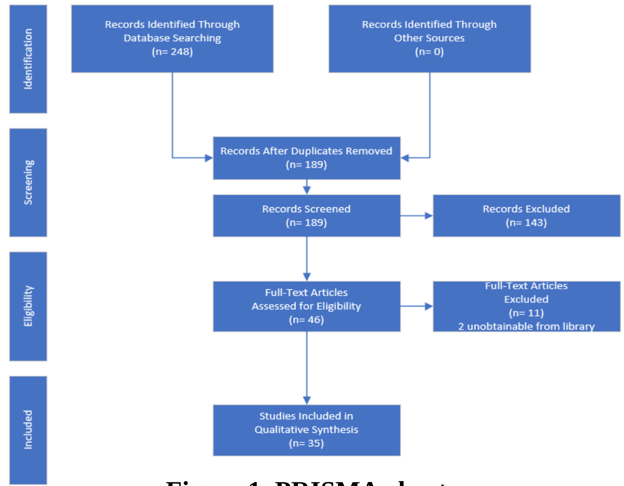

Figure 1. PRISMA chart

The following features were extracted and classified from each of the included studies to answer each of the research questions posited in Table 1. The studies that met the inclusion criteria were summarized based on attributes laid out in Table 1.

Table 1. Question and attribute table

Research Question	Category	Feature	Description
(1) What GANs are being used for tumor-related tasks?	Problem	Medical task	Medical task performed
		Anatomical site	Organ or body area
(2) What modalities are being used most frequently with the application of GANs and their variants?	Input	Image type	Modality used in the study
		Dataset used	Data type and name
(3) Which GAN architectures are used and what are the most prevalent?	Process	GAN variant	Type of GAN
(4) What visualization method was used for interpretation?	Output	Visualization	Technique used for interpretation of the GAN

LITERATURE REVIEW

Previous literature in the field focuses on the broader topic of GANs in medical imaging and creating artificial images for radiology applications using GANs (Sorin et al., 2020; Yi et al., 2019). Another paper investigates a similar issue from a different perspective by looking into general deep learning models applied to electronic health records (Xiao et al., 2018). Previous papers have not investigated which variants are being used to solve specific tumor-related problems. In (Aggarwal et al., 2021), the authors discuss the current state of GANs in their paper and detail an increase in articles written from 378 in 2019 to 1392 in 2020. While there is an increase in articles, there are no distinct review articles that investigate specific applications and visualization of GANs or their variants and how they are used to solve that problem in the tumor problem domain.

GANs and their extensions have carved open many exciting ways to tackle well-known and challenging medical image analysis problems such as medical image de-noising, reconstruction, segmentation, data simulation, detection or classification (Kazeminia et al., 2020). The improvements being made in this study area are due to: (1) GANs maximizing the probability density over the data generating distribution by exploiting density ratio estimation (Isola et al., 2017) in an indirect fashion of supervision; and (2) GANs can discover the high dimensional latent distribution of data, which has led to significant performance gains in the extraction of visual features (Kazeminia et al., 2020). These improvements are helpful, but significant research must be completed further to understand the implementation and utility of their variants.

RESULTS

The search resulted in 248 studies. Fifty-nine duplicate records were removed. The screening stage involved a title and abstract review of the remaining 198 records resulting in 143 exclusions. The eligibility process started with 46 articles for the full review. Eleven articles did not qualify after further review. There were 35 studies included in the detailed literature review.

The most frequent dataset was generalized as patient data with a frequency of 37%. These studies incorporated a patient study. This was the most frequent due to the researcher's access to patient data and patients. The second most frequent dataset was the use of BRATS (Brain Tumor Segmentation) at 23%. The anatomical site most frequently investigated is the brain with 45% of occurrences. The second is lung at 14% and the third is breast at 11%.

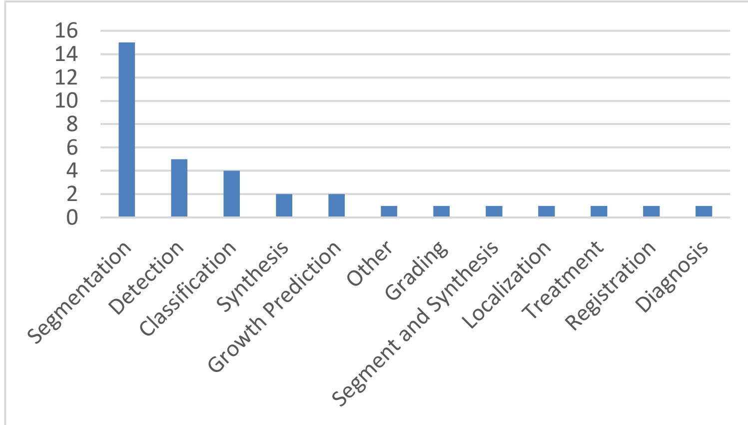

Figure 2. GAN tasks used in papers

Figure 2 shows the frequency of articles by the medical task. The most common task GANs were involved with was related to tumor segmentation with 43%. Tumor detection and classification were the second and third with 14% and 11%, respectively. Tumor synthesis and growth prediction individually made up 5% of the tasks. The remaining tasks individually made up 3% of the tasks investigated.

Figure 3 shows the modality frequency for each article. Magnetic resonance imaging (MRI) and computed tomography (CT) were the most used image inputs with 49% and 26%, respectively. Two modalities were tied for the third, which were multi-modal and mammograms, individually ranking at 6%.

Conditional GAN (cGAN) was the most frequently employed technique at 23%. That variant also was used in 6 different anatomical sites. 46% of the variants used focused on solving the brain tumor task which is the most common problem that researchers investigated. The lung tumor task at 11% was the second most targeted task. This problem has used four different approaches to GAN to solve the problem.

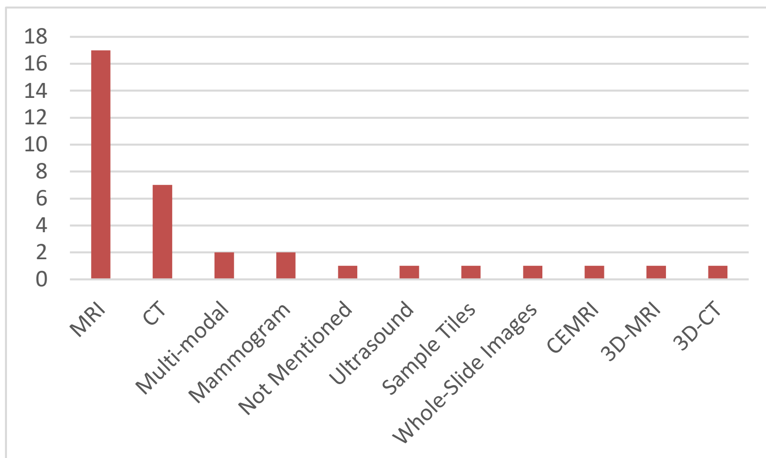

Figure 3. Modalities in papers

Image comparison was the most used visualization measured at 43%. Other studies incorporated some type of image comparison and another type of visualization made up 40%. Other models included AUC charts, loss graphs, ROC charts, and specific measures related to the modalities.

DISCUSSION

Generative adversarial network variants

The most prevalent GAN used was the conditional GAN (cGAN). This was used in tumor segmentation with MRIs and mammograms (B. Yu et al., 2018; Singh et al., 2020), tumor detection with sample tiles (Tavolara et al., 2019), growth prediction using CTs (A. Liebgott et al., 2019), localization with a 3D-CT (Wei et al., 2020), and diagnosis with whole-slide tiles (Rana et al., 2020), suggesting that cGANs may be the most effective GAN used for different types of medical tasks with different types of input modalities. cGANs are used to capture auxiliary information (B. Yu et al., 2018). This variant is broad in nature and has been used to supplement other models (Teki et al., 2019). While benchmarks generally are used to see how well the variant performs, in 50% of the articles that used cGAN, none applied a benchmark to compare to other variants (A. Liebgott et al., 2019; Rana et al., 2020; Wei et al., 2020). Figure 7 presents the other various GAN variants used to solve medical tasks.

The variety of variants that have been used demonstrates that researchers and practitioners are trying to find new ways to achieve the highest performance. Many of the variants used have attempted to combine two or more GAN methods to complete their studies' objective(s). In fact, in 2018, the only published study used cGAN and five studies in 2019 used cGANs. Aside from that, only three studies used GAN without any additional variants (Gao & Wang, 2019; Ghassemi et al., 2020; O'Briain et al., 2020), 77% of the other studies reviewed attempted to use an ensemble GAN technique to achieve higher accuracy. A substantial amount of work has been conducted to optimize GANs by taking on an ensemble approach. High-quality datasets are crucial to tackling smaller datasets that plague the tumor-related research problem domain. For example, (C. Ge et al., 2020) claims that the development of GANs will assist with tackling the commonly encountered problems of insufficiently large brain tumor datasets and incomplete modality of images.

Dataset size and collection method

Very few studies had extensive datasets in each publication. This is to be expected as the primary purpose of GANs is to try to augment the data to provide a larger set of data to work with. Four studies did not report dataset size (Elazab et al., 2020; Lee et al., 2020; N. Xi, 2019; T. E. & K. Saruladha, 2020). The most common dataset size was 200-300 images which accounted for 28% of the articles. Additionally, 69% of the articles studied held less than 1000 images. Many of the GAN variants were developed to better understand and use for specific problem domains.

While performance was reported in all studies, there was no common metric to compare across each study. Therefore, it is not exactly clear whether the size of the study had a significant impact on the findings (Morid et al., 2021). This creates a defined gap in the research where the understanding of optimal dataset thresholds should be understood, analyzed, and reported to understand better if dataset size has a significant effect on the performance of deep learning or machine learning approaches on the replicated datasets created from the GANs. The utility of GAN is not limited by the dataset collection method. 63% of the studies investigated used public data to develop new variants and study current GANs, while the other 37% of the studies used patient data from their organizations.

Visualization techniques

A majority (77%) of the reviewed studies visualized the results through image comparison. About 43% of the studies incorporated just image comparison. The other 34% of the studies incorporated image comparison and a statistical visualization such as a boxplot detailing further details about the technique used. These visualization techniques should be incorporated into any GAN study. They can help provide insight into how well the GAN presented a newly created image based on previous data which will assist with establishing trust in the medical community when considering the utilization of GANs (Borjali et al., 2020).

Research Agenda:

- Further investigation into each anatomical site to understand how each modality reacts to the implementation of GANs.
- Tumor detection and segmentation were the most prevalent tumor-related studies. The other problem domains should be investigated further to see if GANs are as effective in those environments.
- Determine if GANs can augment data from different study modalities.
- Identify the best performing GAN in the relevant study domain.
- Further, investigate the relevance of GANs in radiology information systems.
- Determine whether GANs are generalizable to other tasks in the healthcare domain.
- Develop a framework to formalize GAN development and allow for generalizability.
- Identify whether there is an optimal size of the dataset and its impacts on GAN performance.
- Determine which is the most effective visualization for GAN troubleshooting and development.

This study yielded significant results but still had some limitations. Many problem domains regarding image modality and the anatomical site had limited studies completed. A single researcher classified and identified each article during the systematic review. The systematic literature review was also limited by only having access to Academic Search Premier, Association for Computing Machinery, Business Source Premier, IEEE, PubMed, and ScienceDirect. Future research should address the agenda items posited to begin furthering information system research into GANs.

CONCLUSION

The current state of the literature shows there are still significant contributions to the GAN and tumor-related field. Significant benefits of using GANs in tumor-related research are the ability to synthesize data, augment data, and create synthetic data to more successfully train and test models. Given the popularity of GANs and how significant tumor-related research is, in-depth research on this topic is quite limited. Understanding the benefits in depth and addressing the items in the research agenda will enable GANs to be effectively implemented into tumor and health related research.

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