

Adversarial Attacks Against Medical Deep Learning Systems

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ABSTRACT

The discovery of adversarial examples has raised concerns about the practical deployment of deep learning systems. In this paper, we demonstrate that adversarial examples are capable of manipulating deep learning systems across three clinical domains. For each of our representative medical deep learning classifiers, both white and black box attacks were highly successful. Our models are representative of the current state of the art in medical computer vision and, in some cases, directly reflect architectures already seeing deployment in real world clinical settings. In addition to the technical contribution of our paper, we synthesize a large body of knowledge about the healthcare system to argue that medicine may be uniquely susceptible to adversarial attacks, both in terms of monetary incentives and technical vulnerability. To this end, we outline the healthcare economy and the incentives it creates for fraud and provide concrete examples of how and why such attacks could be realistically carried out. We urge practitioners to be aware of current vulnerabilities when deploying deep learning systems in clinical settings, and encourage the machine learning community to further investigate the domain-specific characteristics of medical learning systems.

CCS CONCEPTS

• **Computing methodologies** → **Neural networks**; • **Applied computing** → **Health informatics**; • **Security and privacy** → *Economics of security and privacy.*

KEYWORDS

adversarial examples, healthcare, deep learning, neural networks, security

1 INTRODUCTION

Over the past seven years, deep learning has transformed computer vision and has been implemented in scores of consumer-facing products. Many are excited that these approaches will continue to expand in scope and that new tools and products will be improved through the use of deep learning. One particularly exciting application area of deep learning has been in clinical medicine. There are

many recent high-profile examples of deep learning achieving parity with human physicians on tasks in radiology [21, 56], pathology [9], dermatology [19], and ophthalmology [25]. In some instances, the performance of these algorithms exceed the capabilities of most individual physicians in head-to-head comparisons. This has led some to speculate that entire specialties in medical imaging, such as radiology and pathology, may be radically reshaped [27] or cease to exist entirely. Furthermore, on April 11, 2018, an important step was taken towards this future: the U.S. Food and Drug Administration announced the approval of the first computer vision algorithm that can be utilized for medical diagnosis without the input of a human clinician [3].

In parallel to this progress in medical deep learning, the discovery of so-called ‘adversarial examples’ has exposed vulnerabilities in even state-of-the-art learning systems [22]. Adversarial examples – inputs engineered to cause misclassification – have quickly become one of the most popular areas of research in the machine learning community [41, 42, 49, 61]. While much of the interest with adversarial examples has stemmed from their ability to shed light on possible limitations of current deep learning methods, adversarial examples have also received attention because of the cybersecurity threats they may pose for deploying these algorithms in both virtual and physical settings [7, 12, 24, 32, 39, 49].

Given the enormous costs of healthcare in the US, it may seem prudent to take the expensive human ‘out of the loop’ and replace him or her with an extremely cheap and highly accurate deep learning algorithm. This seems especially tempting given a recent study’s finding that physician and nursing pay is one of the key drivers of high costs in the US relative to other developed countries [46]. However, there is an under-appreciated downside to widespread automation of medical imaging tasks given the current vulnerabilities of these algorithms. If we seriously consider taking the human doctor completely ‘out of the loop’ (which now has legal sanction in at least one setting via the FDA, with many more to likely follow), we are forced to also consider how adversarial attacks may present new opportunities for fraud and harm. In fact, even with a human in the loop, any clinical system that leverages a machine learning algorithm for diagnosis, decision-making, or reimbursement could be manipulated with adversarial examples.

In this paper, we extend previous results on adversarial examples to three medical deep learning systems modeled after the state of

the art medical classifiers. On the basis of these results and knowledge of the healthcare system, we argue that medical imaging is particularly vulnerable to adversarial attacks and that there are potentially enormous incentives to motivate prospective bad actors to carry out these attacks. We hope that by highlighting these vulnerabilities, more researchers will explore potential defenses against these attacks within the healthcare domain. Because the healthcare system is complex and administrative processes can appear byzantine, it may be difficult to imagine how these attacks could be operationalized. To ground these abstract potentials for harm in actual use cases, we describe realistic scenarios where clinical tasks might rely on deep learning and give specific examples of the fraud that could be mediated by adversarial attacks. Our goal is to provide background on the distinct features of the medical pipeline that make adversarial attacks a threat, and also to demonstrate the practical feasibility of these attacks on real medical deep learning systems.

1.1 Adversarial Examples

Adversarial examples are inputs to machine learning models that have been crafted to force the model to make a classification error. This problem extends back in time at least as far as the spam filter, where systematic modifications to email such as ‘good word attacks’ or spelling modifications have long been employed to try to bypass the filters [16, 34, 35]. More recently, adversarial examples were re-discovered and described in the context of deep computer vision systems through the work of Szegedy et al. [61] and Goodfellow et al. [22]. Particularly intriguing in these early examples was the fact that adversarial examples could be crafted to be extremely effective despite being imperceptibly different from natural images to human eyes. In the years since, adversarial examples – visible and otherwise – have been shown to exist for a wide variety of classic and modern learning systems [12, 18, 48]. By the same token, adversarial examples have been extended to various other domains such as text and speech processing [14, 28]. For an interesting history of adversarial examples and methods used to combat them see Biggio and Roli [10].

Figure 1 places adversarial attacks within the broader context of machine learning development and deployment. While there are many possible intentional and inadvertent failures of real-world machine learning systems, adversarial attacks are particularly important to consider from the standpoint of model deployment, because they enable those submitting data into a running ML algorithm to subtly influence its behavior without ever achieving direct access to the model itself or the IT infrastructure that hosts it.

Adversarial examples are generally thought to arise from the piecewise linear components of complex nonlinear models [22]. They are not random, they are not due to overfitting or incomplete model training, they occupy only a comparatively small subspace of the feature landscape, they are robust to random noise, and they have been shown to transfer in many cases from one model to another [48, 62]. Furthermore, in addition to executing many successful attacks in purely virtual settings, researchers in the past several years have also demonstrated that adversarial attacks can generalize to physical world settings [7, 12, 20, 32].

One natural question raised by the existence of adversarial examples is to what extent and in what forms they constitute a viable risk for harm in real-world machine learning settings. Many authors have discussed the feasibility of and possible motivations for adversarial attacks on certain real-world systems such as self-driving cars [15, 20, 36]. However, to our knowledge, previous machine learning literature has yet to thoroughly discuss the possibility of adversarial attacks on medical systems.

2 IDENTIFYING FACTORS IN THE U.S. HEALTHCARE SYSTEM THAT FAVOR ADVERSARIAL ATTACKS

In this section, we provide a synthesis of aspects of the healthcare system that may create both the incentive and the opportunity for a bad actor to carry out an adversarial attack.

2.1 Background on the healthcare economy and possible incentives for fraud via adversarial attacks

The healthcare economy is huge and fraud is already pervasive. The United States spent approximately \$3.3 trillion (17.8% of GDP) on healthcare in 2016 [46], and healthcare is projected to represent 1/5 of the US economy by 2025. Given the vast sums of money represented by the healthcare economy, inevitably some seek to profit by committing fraud against the healthcare system. Medical fraud is estimated to cost hundreds of billions of dollars each year, and one study estimated this number to be as high as \$272 billion in 2011 [26]. Fraud is committed both by large institutions and by individual actors. Large institutions engage in fraud by systemically inflating costs for services to increase revenue [51, 58]. Likewise, it has been found that some individual physicians routinely bill for the highest allowable amount over 90% of the time [45].

Algorithms will likely make medical reimbursement decisions in the future. Due to the amount of money involved with the delivery of healthcare, complex book-keeping systems have been created to facilitate billing and reimbursement. In fact, most of the data generated by the healthcare system in the electronic healthcare record (EHR) is created to justify payments from ‘payers’ (private or public insurers) to ‘providers’ (hospitals and physicians). In many cases, the level of monetary reimbursement for a given patient hinges on the establishment of specific diagnostic ‘codes’, which are used to record a patient’s diagnoses and treatments with high granularity¹[59]. In an effort to increase revenue, some providers engage in the practice of ‘upcoding’ diagnoses or procedures – selecting the codes which will allow them to bill for the highest amount. For their part, insurance companies seek to minimize total expenditure by investing millions of dollars in IT and personnel to identify unjustified billing codes. The resultant struggle between payors and providers has been extensively documented [30, 65]. To ensure consistency and justifiability, insurance companies will often demand specific gold standard tests as proof of diagnosis before reimbursing a given medical claim, and leverage increasingly

¹See for instance the International Classification of Disease code V97.33XD, which represents the following diagnosis: ‘Sucked into jet engine, subsequent encounter’

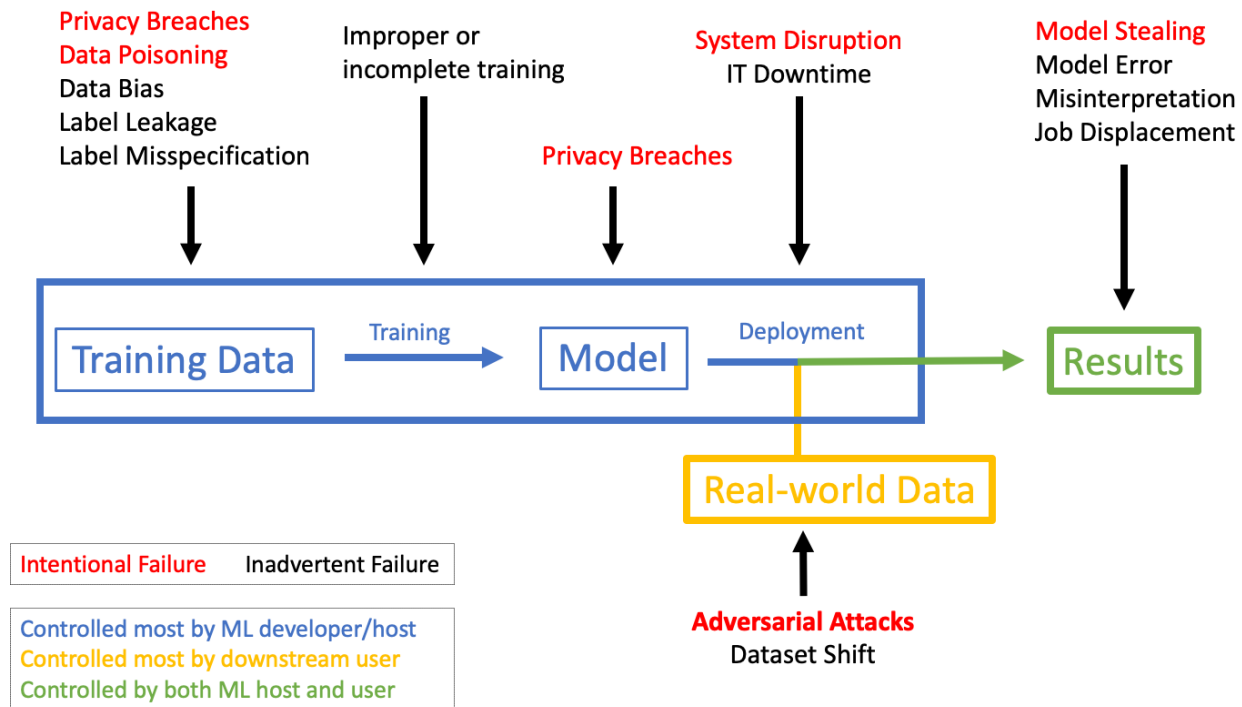


Figure 1: Adversarial attacks within the broader taxonomy of risks facing the machine learning pipeline. Adversarial attacks pose just one of many possible risks in the development and deployment of ML systems, but are noteworthy because they enable end-users to manipulate model outputs without ever influencing the training process or gaining access to the deployed model itself.

sophisticated analytics to determine reimbursement value. Given these dynamics, it is seemingly inevitable that insurance companies will begin to require algorithmic confirmation of certain diagnoses before providing reimbursement. If and when this occurs, the ability to undetectably influence (either as a provider or as a payer) the outputs of trusted and otherwise unbiased diagnostic systems would result in the ability to influence the movement of billions of dollars through the healthcare economy. Even today, the practice of upcoding, which often entails finding subtle combinations of codes that influence reimbursement [57], can itself be arguably considered a form of adversarial attack against reimbursement algorithms.

Algorithms will increasingly determine pharmaceutical and device approvals. The monetary value of a successful clinical trial is immense, with one recent study estimating the median revenue across individual cancer drugs to be as high as \$1.67 billion only four years after approval [53]. At the same time, regulatory bodies such as the FDA are increasingly allowing for the approval of new drugs based on digital *surrogates* for patient response, including medical imaging [52]. As algorithmic endpoints for clinical trials become increasingly accepted – and deep learning algorithms continue to assert themselves as equal or superior to humans on well-defined visual diagnostic tasks – we could soon reach a future where billion dollar drug decisions are made primarily by machines.

In such a future, effectively executed adversarial attacks could allow trialists to imperceptibly ‘put their thumb on the scale,’ even if images are vetted to ensure they are coming from the correct patients.

2.2 Distinctive technical sources of vulnerability to adversarial attacks among medical machine learning systems

Ground truth is often ambiguous. Compared to most common image classification tasks, the ground truth in medical imaging is often controversial, with even specialty radiologists disagreeing on well defined tasks [11, 33, 43]. As such, if end-users selectively perturb images for which it is difficult to establish the true diagnosis, they can make it extremely difficult to detect their influence through even expert human review. Somewhat ironically, it is these borderline cases are where deep learning is likely to be most valuable.

Medical imaging is highly standardized. Compared to other domains of computer vision, medical imaging is extremely standardized, with images generally captured with pre-defined and well-established positioning and exposure [60]. As such, medical adversarial attacks do not need to meet the same standards of invariance to lighting and positional changes as attacks on other real-world systems such as self-driving cars. This is potentially

important, as some have argued that dynamic viewing conditions imply that ‘there is a good prospect that adversarial examples can be reduced to a curiosity with little practical impact’ [36].

Commodity network architectures are often used. Nearly all of the most successful published methods in medical computer vision have consisted of the same fundamental architecture: one of a small set of pretrained ImageNet models that was fine-tuned to the specific task [19, 25, 64]. This lack of architectural diversity could make it easier for potential attackers to build transferable attacks against medical systems. By the same token, given the importance of peer review and publication in validating and approving medical diagnostics, it is likely the architectures of most medical image classification models will be public for the sake of transparency, allowing for more targeted adversarial attacks.

Medical data interchange is limited and balkanized. Five electronic health record (EHR) vendors constitute about half of the market and hundreds of others serve the other half. Even within an EHR vendor, data sharing is spotty and the terminologies and their semantics vary considerably from one implementation to another. On the one hand, this means that there are no universally shared mechanisms for authentication, verification of message integrity, data quality metrics, nor mechanisms for automated oversight. On the other hand, this allows healthcare providers to customize their EHR’s, billing, and other information technology systems in ways that are opaque to most external auditors using one-size-fits-all tools and methods.

Hospital infrastructure is very hard to update. Medical software is often implemented within monolithic enterprise-wide proprietary software systems, making updates, revisions and fixes expensive and time-consuming. For context, consider the coding dictionaries used to classify patients’ diseases, the International Classification of Disease (ICD) system. As recently as 2013, most hospitals were operating using the ninth edition of this coding scheme, published in 1978, despite the fact that a revised version (ICD-10) was published in 1990. All told, the conversion to the ICD-10 coding scheme has been estimated to cost major health centers up to \$20 million *each* and require up to 15 years [59]. Others decided in the early 2000s that it would be preferable to skip the 1990 schema entirely and wait for ICD-11, despite the fact that its release wasn’t scheduled until 2018. Thus, vulnerabilities present in medical software are likely to persist for years due to the difficulty and expense involved with update hospital infrastructure.

Medicine contains a mix of technical and non-technical workers. Compared to many other industries, medicine is extremely interdisciplinary and mostly comprised of members who lack a strong computational or statistical training background. For example, in the case of self-driving cars, the teams developing computer vision systems are likely to be led and staffed primarily by engineers, if not computer scientists. In contrast, since the clinical usability of medical imaging systems is also extremely important, hospitals are likely to lean heavily on physician-researchers in developing these systems, who tend to lack robust computational expertise [38].

Biomedical images carry personal signatures that could be used to defend against many simpler attacks, but not against adversarial examples. One potential alternative to adversarial attacks on part of malicious end-users would be to simply substitute

in true images of the target class. However, biomedical images – including retinal images, X-rays, and skin photographs – are often as unique to their owners as fingerprints [4, 40, 54]. This provides several advantages against substitution attacks: First, algorithms could be designed to check input images against prior images from the same patient, to ensure that their identities match. Second, algorithms could query against the database of previously submitted images and flag any inputs that are likely from the same patients as previous entries. Both strategies would make it more difficult for fraudsters to continually execute substitution attacks against ML systems, but neither would defend against adversarial attacks, which needn’t change the personal identifiers in the image. By analogy, adversarial attacks applied to billing codes or medical text could serve to manipulate reimbursement algorithms by selecting combinations of codes or words that are individually truthful but in combination yield anomalously high reimbursement.

There are many potential adversaries. The medical imaging pipeline has many potential attackers and is thus vulnerable at many different stages. While in theory one could devise elaborate image verification schemes throughout the data processing pipeline to try to guard against attacks, this would be extremely costly and difficult to implement in practice.

3 ATTACKING REPRESENTATIVE CLINICAL DEEP LEARNING SYSTEMS

To demonstrate the feasibility of medical adversarial attacks, we developed a series of medical classifiers modeled after state-of-the-art clinical deep learning systems, and launched successful white- and black-box attacks against each.

3.1 Methods

3.1.1 Construction of medical classification models. We developed baseline models to classify referable diabetic retinopathy from retinal funduscopy (similar to Gulshan et al. [25]), pneumothorax from chest-xray (similar to Wang et al. [64] and Rajpurkar et al. [56]), and melanoma from dermoscopic photographs (similar to Esteva et al. [19]). The decision to build models for these particular tasks was made both due to public data availability, as well as the fact that they represent three of the most highly visible successes for medical deep learning.

All of our models were trained on publicly available data. For diabetic retinopathy, this was the Kaggle Diabetic Retinopathy dataset [2]. The key distinction with the Kaggle dataset, however, was that we were seeking to predict *referable* (grade 2 or worse) diabetic retinopathy in accordance with Gulshan et al. [25] rather than predicting the retinopathy grade itself as was the case in the Kaggle competition. As such, the training and test sets from the kaggle competition were merged, relabeled using their provided grades, and split by patient into training and test sets with probability 0.88/0.12. For the chest x-rays, we used the ChestX-Ray14 dataset described by Wang et al. [64]. We identified cases and controls by selecting images whose labels contained ‘pneumothorax’ or ‘no finding’, respectively, and additionally excluded from our control group any images from patients who had received both labels. We then split by patient into training and test sets with probability 0.85/0.15. For melanoma, we downloaded images labeled as benign

or malignant melanocytic lesions from the International Skin Imaging Collaboration website [1], splitting again into training and test sets with probability 0.85/0.15.

As in the case of all three of the original papers that inspired these models, we built our classifiers by fine-tuning a pretrained ImageNet model. For convenience and consistency, we chose to build each of our networks using a pretrained ResNet-50 model, fine-tuned in Keras using stochastic gradient descent with a learning rate of $1E-3$ and Momentum of 0.9. Data was augmented using 45° rotation and horizontal flipping chest x-ray images, and with 360° rotation, vertical and horizontal flipping, and mixup [66] for funduscopy and dermoscopy images. In all three cases, these settings provided respectable performance and we therefore didn't perform dedicated hyperparameter optimization.

3.1.2 Construction of adversarial attacks. To demonstrate the vulnerability of our models to adversarial attacks under a variety of threat models, we implemented both human-imperceptible and patch attacks.

For our human-imperceptible attacks, we followed the white and black box PGD attack strategies published in Madry et al. [37], which were also described as baselines in Kannan et al. [29]. The PGD attack (see Madry et al. [37] and also Kurakin et al. [32]) is an iterative extension of the canonical fast gradient sign method (FGSM) attack developed by Goodfellow et al. [22]. In the PGD attack, given input $x \in \mathbb{R}^d$, loss function $L(\theta, x, y)$, and a set of allowed perturbations $\mathcal{S} \subseteq \mathbb{R}^d$ (most commonly the ℓ_∞ ball around x), one can perform a projected gradient descent on the negative loss function:

$$x^{t+1} = \Pi_{\mathcal{S}}(x^t + \epsilon \text{sgn}(\nabla_x L(\theta, x, y)))$$

in order to identify an optimal perturbation. We implemented the PGD attack using the library Cleverhans, conducting 20 iterations with hyperparameter $\epsilon = 0.02$ (ϵ corresponds to the maximum permitted ℓ_∞ norm of the perturbation) [47].

For our adversarial patch attacks, we followed the approach of Brown et al. [12]. The learning process of the adversarial patch \hat{p} uses a variant of the expectation over transformation algorithm (originally proposed by Athalye et al. [6]), which can be expressed as the following maximization:

$$\hat{p} = \arg \max_p \mathbb{E} [\log p_{Y|X}(\hat{y} | A(p, X, L, T))] \quad (1)$$

where $p_{Y|X}(\cdot|\cdot)$ represents the probability output from the classifier given the input image X , L is the location of the patch, T is the transformation (rotation and scaling), \hat{y} is the target label (for our application binary label), and $A(\cdot, \cdot, \cdot, \cdot)$ is the deterministic mapping of given image, patch, location and transformation into the adversarially patched input image. The expectation is over the locations, transformations and input images, thus allowing the resulting patch to be 'universal,' because it was trained over the entire training set and robust since training averaged over various location and transformations. We deployed adversarial patches with scaling parameter 0.4.

White box attacks for each attack were implemented by building attacks directly on the victim model itself. As in Madry et al. [37]

and Kannan et al. [29], black box attacks were performed by crafting the attack against an independently-trained model with the same architecture and then transferring the resultant adversarial examples to the victim.

Finally, as a control, we implemented a naive patch attack using natural images, as in Brown et al. [12]. To make this as strong a baseline as reasonably possible, we built our natural image patches using the images assigned by the model with the highest probability of the target class. Resultant patches were then applied to the test set images with random rotation and scaling factor 0.4, so match the adversarial patch.

Availability of code: Code to reproduce the analyses and results can be found at the first author's Github account:

<https://github.com/sgfin/adversarial-medicine>.

3.2 Results

The results of our experiments are depicted in Table 1 and in Figure 2.

While discrepancies in data source and train-test partitioning makes direct comparison to state-of-the-art models unfeasible, all of our baseline models achieved performance reasonably consistent with the results reported in the original manuscripts on natural images: AUROC of 0.910 for diabetic retinopathy compared with 0.936 reported in Gulshan et al. [25], AUROC of 0.936 for pneumothorax compared with 0.90 reported by Rajpurkar et al. [56], and AUROC of 0.86 on melanoma compared with 0.91-0.94 reported in Esteva et al. [19].

Projected gradient descent attacks, targeting the incorrect answer in every case, produced effective AUROCs of 0.000 and accuracies of 0% for all white box attacks. Black box attacks produced AUROCs of less than 0.10 for all tasks, and accuracies ranging from 0.01% on funduscopy to 37.9% on dermoscopy. Qualitatively, all attacks were human-imperceptible.

Adversarial patch attacks also achieved effective AUROCs of 0.000 and accuracies of <1% for white box attacks on all tasks. Black box adversarial patch attacks achieved AUROCs of less than 0.005 for all tasks and accuracies less than 10%. The "natural patch" controls created by adding patches created from the most-strongly classified image of the desired class resulted in AUROCs ranging from 0.48-0.83 with accuracies ranging from 67.5% to 92.1%.

4 DISCUSSION

Our experiments indicate that adversarial attacks are likely to be feasible even for extremely accurate medical classifiers, regardless of whether prospective attackers have direct access to the model or require their attacks to be human imperceptible. Of note, while the PGD attacks require digital access to the specific images to be sent into the model, adversarial patch attacks are universal in the sense that they can be applied to any image. This could open the possibility for implementation of attacks upstream from the image capture itself, rendering data processing defenses such as image hashing at point-of-capture ineffective. In addition, it is noteworthy to recognize that adversarial patches were far more potent than "photoshop"-style natural patch attacks that alter the image using the most strongly classified image from the training set.

Input Images	<i>Fundoscopy</i>			<i>Chest X-Ray</i>			<i>Dermoscopy</i>		
	Accuracy	AUROC	Avg. Conf.	Accuracy	AUROC	Avg. Conf.	Accuracy	AUROC	Avg. Conf.
Clean	91.0%	0.910	90.4%	94.9%	0.937	96.1%	87.6%	0.858	94.1%
PGD - White Box	0.00%	0.000	100.0%	0.00%	0.000	100.0%	0.00%	0.000	100.0%
PGD - Black Box	0.01%	0.002	90.9%	15.1%	0.014	92.6%	37.9%	0.071	92.0%
Patch - Natural	78.5%	0.828	80.8%	92.1%	0.539	95.8%	67.5%	0.482	85.6%
Patch - White Box	0.3%	0.000	99.2%	0.00%	0.000	98.8%	0.00%	0.000	99.7%
Patch - Black Box	3.9%	0.000	97.5%	9.7%	0.004	83.3%	1.37%	0.000	97.6%

Table 1: Results of medical deep learning models on clean test set data, white box, and black box attacks.

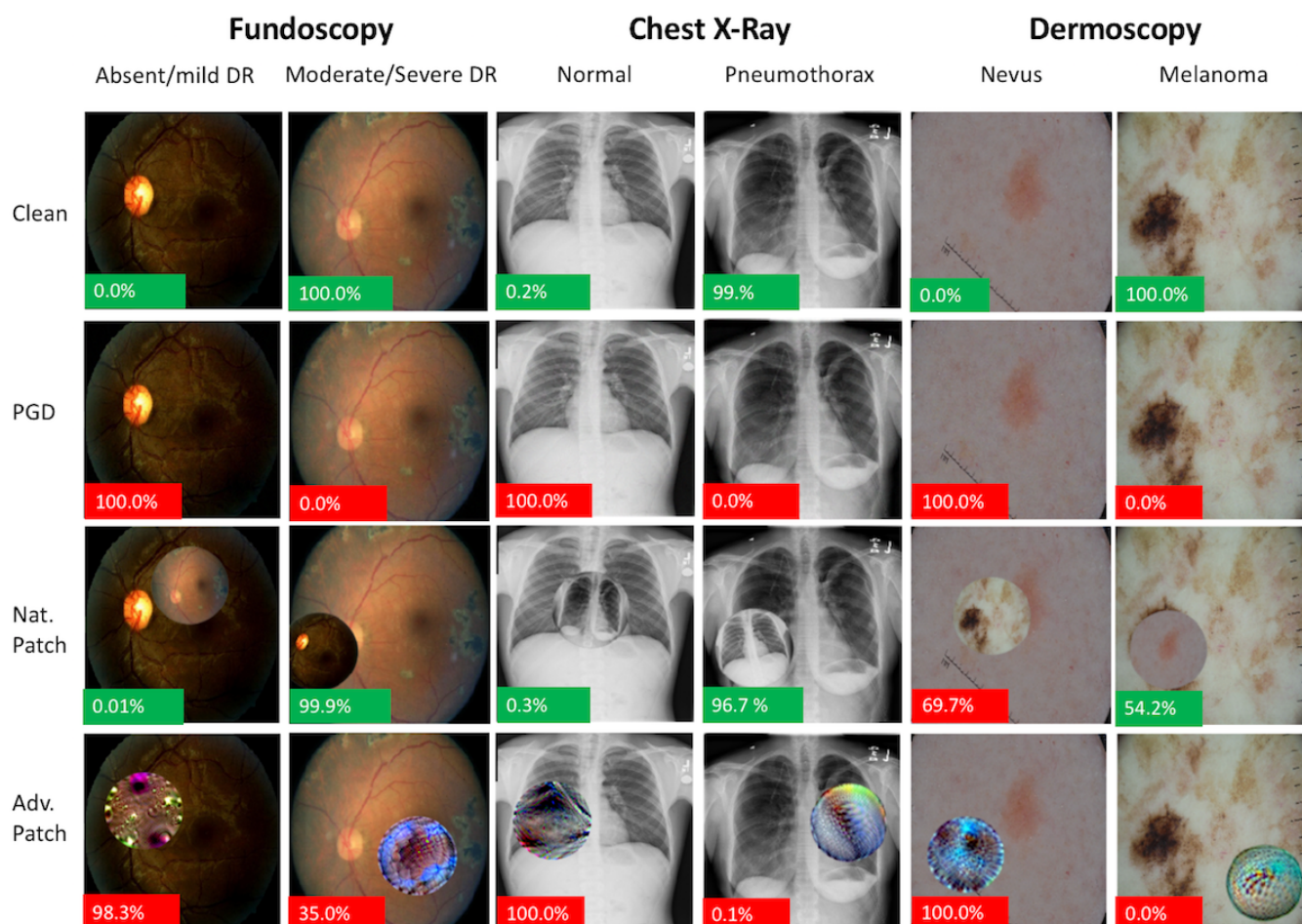


Figure 2: Characteristic results of adversarial manipulation. Each clean image represents the natural image to which the model assigns the highest probability for the given diagnosis. The percentage displayed on the bottom left of each image represents the probability that the model assigns that image of being diseased. Green = Model is correct on that image. Red = Model is incorrect.

We now discuss how someone might perform adversarial attacks against the systems developed in previous section under a realistic set of conditions. As stated above, we focus this discussion on imaging-based ML models, though similar arguments apply to adversarial examples crafted on billing code submissions or medical text. For the purposes of illustration, consider a scenario where the

ML models have been subjected to extensive testing and validation and are now clinically deployed. These systems would function much like laboratory tests do now and provide confirmation of suspected diagnoses. In some instances, an insurance company may require a confirmatory diagnosis from one of these systems in order for a reimbursement to be made. Further, the insurance company or

regulatory agency may have separate methods deployed to ensure the patient identity matches from prior images or has never been submitted from the same provider before. We provide the examples below to show that in many instances there is both the *opportunity* and *incentive* for someone to use an adversarial example to defraud the healthcare system.

4.1 Hypothetical examples

Adversarial examples in dermatology: Dermatology in the US operates under a ‘fee for service’ model wherein a physician or practice is paid for the services or procedures they perform for the patient. Under this model, dermatologists are incentivized to perform as many procedures as possible, as their revenue is directly tied to the amount of procedures they perform. This has caused some dermatologists to perform a huge number of unnecessary procedures to increase revenue. For example, one dermatologist in Florida was recently sentenced to 22 years in prison after performing more than three thousand unnecessary surgical procedures [58]. To combat fraud and unnecessary procedures such as this, an insurance company could require that a deep learning system (e.g. the one from Section 4) analyzes all dermoscopy images to confirm that surgery is necessary. In this scenario, a bad actor could add adversarial noise to images to ensure that the deep learning model always gives the diagnosis that he or she desires. Furthermore, they could add this noise to ‘borderline’ cases, which would render the attack nearly impossible to detect by human review. Thus, a bad actor like the Florida dermatologist from [58] could sidestep an insurance company’s image-based fraud detector and continue to defraud the system in perpetuity.

Adversarial examples in radiology. Thoracic radiology images (typically CT scans, which is a 3D application of X-Ray technology) are also often used to measure tumor burden, a common secondary endpoint of cancer therapy response [52]. To foster more rapid and more universally standardized clinical trials, the FDA might consider requiring that trial endpoints, such as tumor burden in chest imaging, be evaluated by a deep learning system such as the one from Section 4. By applying undetectable adversarial perturbations to the images, a company running a trial could effectively guarantee a positive trial result with respect to this endpoint, even if images are subsequently released to the public for inspection. In addition, chest X-rays provide a common screening test for dozens of diseases, and a positive chest X-ray result is often used to justify more heavily reimbursed procedures such as biopsies, CT or MR imaging, or surgical resection. As such, one could imagine many scenarios arising around chest X-rays that are directly analogous to the melanoma detection situation described above.

Adversarial examples in ophthalmology. As described in Section 3, providers and pharmaceutical companies are not the only organizations that could be incentivized to employ adversarial manipulation. Often, the entities who pay for healthcare (such as private or public insurers) wish to curtail the utilization rates of certain procedures to reduce costs. However, there are often guidelines from government agencies (such as the Centers for Medicare and Medicaid Services) that specify diagnostic criteria which if present dictate that certain procedures must be covered. One such criterion could be that any patient with a confirmed diabetic retinopathy

diagnosis from a deep learning system such as the one from Section 4 must have the resulting vitrectomy surgery covered by their insurer. Even though the insurer has no ability to control the policy, they could still control the rate of surgeries by applying adversarial noise to mildly positive images, reducing the number of procedures. On the other end of the spectrum, an ophthalmologist could affix a universal adversarial patch to the lens of his image capture system, forcing a third party image processing system to mistake all images for positive cases without having to make any alterations to the image within the IT system itself.

4.2 Possible areas for further research

We hope that our discussion and demonstrations can help motivate further research into adversarial examples generally as well as within the specific context of healthcare. In particular, we consider the following areas to be of high priority:

Algorithmic defenses against adversarial examples remain an extremely open and challenging problem. We defer a full discussion of the extremely rapidly evolving field of adversarial defenses to the primary literature [13, 17, 22, 29, 31, 31, 37, 48, 49, 55, 61, 62]. Unfortunately, despite the explosive emergence of defense strategies, there does not appear to be a simple and general algorithmic fix for the adversarial problem available in the short term. For example, one recent analysis investigated a series of promising methods that relied on gradient obfuscation, and demonstrated that they could be quickly broken [5]. Despite this, we also note that principled approaches to adversarial robustness are beginning to show promise. For example, several papers have demonstrated what appears to be both high accuracy and strong adversarial robustness on smaller datasets such as MNIST, [29, 37], and there have also been several results including theoretical *guarantees* of adversarial robustness, albeit on small datasets and/or with still-insufficient accuracy [31]. Generalized attempts at algorithmic robustness are promising, but have yet to provide methods that can demonstrate high levels of both accuracy and adversarial robustness at ImageNet scale. However, **domain-specific algorithmic** defenses such as dataset-specific image preprocessing have been shown to be highly effective on some datasets [23]. In this light, particularly given the highly standardized image capture procedures in biomedical imaging, we feel that medical-domain-specific algorithmic defenses offer an important and promising area of future research.

Infrastructural defenses against clinical adversarial attacks include methods deployed to prevent potential bad actors from altering medical images – or at least make it easier to confirm image tampering if adversarial examples are suspected. For example, imaging devices could immediately store a hashed version of any image they generate, which could subsequently be used as a reference. Likewise, raw clinical images could be processed and analyzed on a third-party system to prevent any possible systemic manipulation by payers or providers. This family of approaches to standardized best practices is reminiscent of the system of Clinical Laboratory Improvement Amendments (CLIA), a set of federal policies that regulates the process by which clinical laboratory samples are handled and analyzed in the United States [44]. Given that algorithmic defenses against adversarial attacks are still very much an area of research, we feel that infrastructural defenses should be strongly

considered for all medical classifier systems that could carry incentives for adversarial attacks. However, implementing healthcare system-wide standardization to this end represents an immense challenge that will require buy-in from both the medical and CS communities.

Ethical tradeoffs are introduced by adversarial examples. As outlined above, several papers have demonstrated greater improvements in adversarial robustness that come at a cost of lower accuracy [50, 63]. However, in medical imaging, this introduces an ethical conundrum: how does one weigh protecting against adversarial examples against any inaccurate diagnosis? Quantifying and making this trade-off explicit would allow for more informed decision making and system design.

5 CONCLUSION

The prospect of improving healthcare and medicine with the use of deep learning is truly exciting. There is reasonable cause for optimism that these technologies can improve outcomes and reduce costs, if judiciously implemented [8]. In this light, it is unsurprising that dozens of private companies and large health centers have initiated efforts to deploy deep learning classifiers in clinical practice settings. As such efforts continue to develop, it seems inevitable that medical deep learning algorithms will become entrenched in the already multi-billion dollar medical information technology industry. However, the massive scale of the healthcare economy brings with it significant opportunity and incentive for fraudulent behavior and ultimately, patient harm.

In this work, we have outlined the systemic and technological reasons that cause adversarial examples to pose a disproportionately large threat in the medical domain, and provided examples of how such attacks may be executed. We hope that our results help facilitate a discussion on the threat of adversarial examples among both computer scientists and medical professionals. For machine learning researchers, we recommend research into infrastructural and algorithmic solutions designed to guarantee that attacks are infeasible or at least can be retroactively identified. For medical providers, payers, and policy makers, we hope that these practical examples can motivate a meaningful discussion into how precisely these algorithms should be incorporated into the clinical ecosystem despite their current vulnerability to such attacks.

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REFERENCES

- [1] [n. d.]. International Skin Imaging Collaboration. isic-archive.com
- [2] [n. d.]. Kaggle Diabetic Retinopathy Challenge. <https://www.kaggle.com/c/diabetic-retinopathy-detection/data>
- [3] 2018. Press Announcements > FDA permits marketing of artificial intelligence-based device to detect certain diabetes-related eye problems. <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm604357.htm>.
- [4] M Angyal and K Derczy. 1998. Personal identification on the basis of antemortem and postmortem radiographs. *Journal of Forensic Science* 43, 5 (1998), 1089–1093.
- [5] Anish Athalye, Nicholas Carlini, and David Wagner. 2018. Obfuscated gradients give a false sense of security: Circumventing defenses to adversarial examples. *arXiv preprint arXiv:1802.00420* (2018).
- [6] Anish Athalye, Logan Engstrom, Andrew Ilyas, and Kevin Kwok. 2017. Synthesizing Robust Adversarial Examples. [abs/1707.07397](https://arxiv.org/abs/1707.07397) (2017). *arXiv:1707.07397* <http://arxiv.org/abs/1707.07397>
- [7] Anish Athalye and Ilya Sutskever. 2017. Synthesizing robust adversarial examples. *arXiv preprint arXiv:1707.07397* (2017).
- [8] Andrew L Beam and Isaac S Kohane. 2016. Translating artificial intelligence into clinical care. *Jama* 316, 22 (2016), 2368–2369.
- [9] Babak Ehteshami Bejnordi, Mitko Veta, Paul Johannes van Diest, Bram van Ginneken, Nico Karssemeijer, Geert Litjens, Jeroen AWM van der Laak, Meyke Hermesen, Quirine F Manson, Maschenka Balkenhol, et al. 2017. Diagnostic assessment of deep learning algorithms for detection of lymph node metastases in women with breast cancer. *Jama* 318, 22 (2017), 2199–2210.
- [10] Battista Biggio and Fabio Roli. 2017. Wild Patterns: Ten Years After the Rise of Adversarial Machine Learning. *arXiv preprint arXiv:1712.03141* (2017).
- [11] Charlotte L Brouwer, Roel JHM Steenbakkers, Edwin van den Heuvel, Joop C Duppen, Arash Navran, Henk P Bijl, Olga Chouvalova, Fred R Burlage, Harm Meertens, Johannes A Langendijk, et al. 2012. 3D variation in delineation of head and neck organs at risk. *Radiation Oncology* 7, 1 (2012), 32.
- [12] Tom B Brown, Dandelion Mané, Aurko Roy, Martin Abadi, and Justin Gilmer. 2017. Adversarial patch. *arXiv preprint arXiv:1712.09665* (2017).
- [13] Jacob Buckman, Aurko Roy, Colin Raffel, and Ian Goodfellow. 2018. Thermometer encoding: One hot way to resist adversarial examples. In *International Conference on Learning Representations*.
- [14] Nicholas Carlini, Pratyush Mishra, Tavish Vaidya, Yuankai Zhang, Micah Sherr, Clay Shields, David Wagner, and Wencho Zhou. 2016. Hidden Voice Commands.. In *USENIX Security Symposium*. 513–530.
- [15] Nicholas Carlini and David Wagner. 2017. Towards evaluating the robustness of neural networks. In *Security and Privacy (SP), 2017 IEEE Symposium on*. IEEE, 39–57.
- [16] Nilesh Dalvi, Pedro Domingos, Sumit Sanghai, Deepak Verma, et al. 2004. Adversarial classification. In *Proceedings of the tenth ACM SIGKDD international conference on Knowledge discovery and data mining*. ACM, 99–108.
- [17] Krishnamurthy Dvijotham, Robert Stanforth, Sven Gowal, Timothy Mann, and Pushmeet Kohli. 2018. A Dual Approach to Scalable Verification of Deep Networks. *arXiv preprint arXiv:1803.06567* (2018).
- [18] Gamaleldin F Elsayed, Shreya Shankar, Brian Cheung, Nicolas Papernot, Alex Kurakin, Ian Goodfellow, and Jascha Sohl-Dickstein. 2018. Adversarial Examples that Fool both Human and Computer Vision. *arXiv preprint arXiv:1802.08195* (2018).
- [19] Andre Esteva, Brett Kuprel, Roberto A Novoa, Justin Ko, Susan M Swetter, Helen M Blau, and Sebastian Thrun. 2017. Dermatologist-level classification of skin cancer with deep neural networks. *Nature* 542, 7639 (2017), 115.
- [20] Ivan Evtimov, Kevin Eykholt, Earlene Fernandes, Tadayoshi Kohno, Bo Li, Atul Prakash, Amir Rahmati, and Dawn Song. 2017. Robust physical-world attacks on machine learning models. *arXiv preprint arXiv:1707.08945* (2017).
- [21] William Gale, Luke Oakden-Rayner, Gustavo Carneiro, Andrew P Bradley, and Lyle J Palmer. 2017. Detecting hip fractures with radiologist-level performance using deep neural networks. *arXiv preprint arXiv:1711.06504* (2017).
- [22] Ian J Goodfellow, Jonathon Shlens, and Christian Szegedy. 2014. Explaining and harnessing adversarial examples. *arXiv preprint arXiv:1412.6572* (2014).
- [23] Abigail Graese, Andras Rozsa, and Terrance E Boult. 2016. Assessing threat of adversarial examples on deep neural networks. In *Machine Learning and Applications (ICMLA), 2016 15th IEEE International Conference on*. IEEE, 69–74.
- [24] Kathrin Grosse, Nicolas Papernot, Praveen Manoharan, Michael Backes, and Patrick McDaniel. 2017. Adversarial examples for malware detection. In *European Symposium on Research in Computer Security*. Springer, 62–79.
- [25] Varun Gulshan, Lily Peng, Marc Coram, Martin C Stumpe, Derek Wu, Arunachalam Narayanaswamy, Subhashini Venugopalan, Kasumi Widner, Tom Madams, Jorge Cuadros, et al. 2016. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. *Jama* 316, 22 (2016), 2402–2410.
- [26] Anita Jain, Samiran Nundy, and Kamran Abbasi. 2014. Corruption: medicine's dirty open secret.
- [27] Saurabh Jha and Eric J Topol. 2016. Adapting to artificial intelligence: radiologists and pathologists as information specialists. *Jama* 316, 22 (2016), 2353–2354.
- [28] Robin Jia and Percy Liang. 2017. Adversarial examples for evaluating reading comprehension systems. *arXiv preprint arXiv:1707.07328* (2017).
- [29] Harini Kannan, Alexey Kurakin, and Ian Goodfellow. 2018. Adversarial Logit Pairing. *arXiv preprint arXiv:1803.06373* (2018).
- [30] Aaron S Kesselheim and Troyen A Brennan. 2005. Overbilling vs. downcoding—the battle between physicians and insurers. *New England Journal of Medicine* 352, 9 (2005), 855–857.

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- [31] J Zico Kolter and Eric Wong. 2017. Provable defenses against adversarial examples via the convex outer adversarial polytope. *arXiv preprint arXiv:1711.00851* (2017).
- [32] Alexey Kurakin, Ian Goodfellow, and Samy Bengio. 2016. Adversarial examples in the physical world. *arXiv preprint arXiv:1607.02533* (2016).
- [33] X Allen Li, An Tai, Douglas W Arthur, Thomas A Buchholz, Shannon Macdonald, Lawrence B Marks, Jean M Moran, Lori J Pierce, Rachel Rabinovitch, Alphonse Taghian, et al. 2009. Variability of target and normal structure delineation for breast cancer radiotherapy: an RTOG Multi-Institutional and Multiobserver Study. *International Journal of Radiation Oncology Biology Physics* 73, 3 (2009), 944–951.
- [34] Daniel Lowd and Christopher Meek. 2005. Adversarial learning. In *Proceedings of the eleventh ACM SIGKDD international conference on Knowledge discovery in data mining*. ACM, 641–647.
- [35] Daniel Lowd and Christopher Meek. 2005. Good Word Attacks on Statistical Spam Filters.. In *CEAS*, Vol. 2005.
- [36] Jiajun Lu, Hussein Sibai, Evan Fabry, and David Forsyth. 2017. No need to worry about adversarial examples in object detection in autonomous vehicles. *arXiv preprint arXiv:1707.03501* (2017).
- [37] Aleksander Madry, Aleksandar Makelov, Ludwig Schmidt, Dimitris Tsipras, and Adrian Vladu. 2017. Towards deep learning models resistant to adversarial attacks. *arXiv preprint arXiv:1706.06083* (2017).
- [38] Arjun K Manrai, Gaurav Bhatia, Judith Strymish, Isaac S Kohane, and Sachin H Jain. 2014. Medicine's uncomfortable relationship with math: calculating positive predictive value. *JAMA internal medicine* 174, 6 (2014), 991–993.
- [39] Marco Melis, Ambra Demontis, Battista Biggio, Gavin Brown, Giorgio Fumera, and Fabio Roli. 2017. Is deep learning safe for robot vision? adversarial examples against the icub humanoid. *arXiv preprint arXiv:1708.06939* (2017).
- [40] Philip E Miller, Allen W Rawls, Shrinivas J Pundlik, and Damon L Woodard. 2010. Personal identification using periocular skin texture. In *Proceedings of the 2010 ACM Symposium on Applied Computing*. ACM, 1496–1500.
- [41] Seyed Mohsen Moosavi Dezfouli, Alhussein Fawzi, and Pascal Frossard. 2016. Deepfool: a simple and accurate method to fool deep neural networks. In *Proceedings of 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR)*.
- [42] Anh Nguyen, Jason Yosinski, and Jeff Clune. 2015. Deep neural networks are easily fooled: High confidence predictions for unrecognizable images. In *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*. 427–436.
- [43] CF Njeh. 2008. Tumor delineation: The weakest link in the search for accuracy in radiotherapy. *Journal of medical physics/Association of Medical Physicists of India* 33, 4 (2008), 136.
- [44] US Department of Health, Human Services, et al. 1992. Medicare, Medicaid and CLIA programs: regulations implementing the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Final rule. *Fed Regist* 57, 40 (1992), 7002–7186.
- [45] Charles Ornstein and Ryann Grochowski-Jones. 2018. Top Billing: Meet the Docs who Charge Medicare Top Dollar for Office Visits — ProPublica. <https://www.propublica.org/article/billing-to-the-max-docs-charge-medicare-top-rate-for-office-visits>
- [46] Irene Papanicolas, Liana R Woskie, and Ashish K Jha. 2018. Health care spending in the United States and other high-income countries. *JAMA* 319, 10 (2018), 1024–1039.
- [47] Nicolas Papernot, Nicholas Carlini, Ian Goodfellow, Reuben Feinman, Fartash Faghri, Alexander Matyasko, Karen Hambardzumyan, Yi-Lin Juang, Alexey Kurakin, Ryan Sheatsley, et al. 2016. cleverhans v2. 0.0: an adversarial machine learning library. *arXiv preprint arXiv:1610.00768* (2016).
- [48] Nicolas Papernot, Patrick McDaniel, and Ian Goodfellow. 2016. Transferability in machine learning: from phenomena to black-box attacks using adversarial samples. *arXiv preprint arXiv:1605.07277* (2016).
- [49] Nicolas Papernot, Patrick McDaniel, Xi Wu, Somesh Jha, and Ananthram Swami. 2016. Distillation as a defense to adversarial perturbations against deep neural networks. In *Security and Privacy (SP), 2016 IEEE Symposium on*. IEEE, 582–597.
- [50] Magdalini Paschali, Sailesh Conjeti, Fernando Navarro, and Nassir Navab. 2018. Generalizability vs. Robustness: Adversarial Examples for Medical Imaging. *arXiv preprint arXiv:1804.00504* (2018).
- [51] Kalb PE. 1999. Health care fraud and abuse. *JAMA* 282, 12 (1999), 1163–1168. <https://doi.org/10.1001/jama.282.12.1163> arXiv:/data/journals/jama/4697/jlm90010.pdf
- [52] Homer H Pien, Alan J Fischman, James H Thrall, and A Gregory Sorensen. 2005. Using imaging biomarkers to accelerate drug development and clinical trials. *Drug discovery today* 10, 4 (2005), 259–266.
- [53] Vinay Prasad and Sham Mailankody. 2017. Research and development spending to bring a single cancer drug to market and revenues after approval. *JAMA internal medicine* 177, 11 (2017), 1569–1575.
- [54] Sana Qamber, Zahra Waheed, and M Usman Akram. 2012. Personal identification system based on vascular pattern of human retina. In *Biomedical Engineering Conference (CIBEC), 2012 Cairo International*. IEEE, 64–67.
- [55] Aditi Raghunathan, Jacob Steinhardt, and Percy Liang. 2018. Certified defenses against adversarial examples. *arXiv preprint arXiv:1801.09344* (2018).
- [56] Pranav Rajpurkar, Jeremy Irvin, Kaylie Zhu, Brandon Yang, Hershel Mehta, Tony Duan, Daisy Ding, Aarti Bagul, Curtis Langlotz, Katie Shpanskaya, et al. 2017. CheXNet: Radiologist-Level Pneumonia Detection on Chest X-Rays with Deep Learning. *arXiv preprint arXiv:1711.05225* (2017).
- [57] Kristi Reynolds, Paul Muntner, and Vivian Fonseca. 2005. Metabolic syndrome: underrated or underdiagnosed?
- [58] William J Rudman, John S Eberhardt, William Pierce, and Susan Hart-Hester. 2009. Healthcare fraud and abuse. *Perspectives in Health Information Management/AHIMA, American Health Information Management Association* 6, Fall (2009).
- [59] Tekla B Sanders, Felicia M Bowens, William Pierce, Bridgette Stasher-Booker, Erica Q Thompson, and Warren A Jones. 2012. The road to ICD-10-CM/PCS implementation: forecasting the transition for providers, payers, and other healthcare organizations. *Perspectives in health information management/AHIMA, American Health Information Management Association* 9, Winter (2012).
- [60] George Simon. 1971. *Principles of chest X-ray diagnosis*. Butterworths.
- [61] Christian Szegedy, Wojciech Zaremba, Ilya Sutskever, Joan Bruna, Dumitru Erhan, Ian Goodfellow, and Rob Fergus. 2014. Intriguing properties of neural networks. *arXiv* (2014), 1–10. <https://doi.org/10.1021/ct2009208>
- [62] Florian Tramèr, Nicolas Papernot, Ian Goodfellow, Dan Boneh, and Patrick McDaniel. 2017. The Space of Transferable Adversarial Examples. *arXiv* (2017), 1–15. <http://arxiv.org/abs/1704.03453>
- [63] Dimitris Tsipras, Shibani Santurkar, Logan Engstrom, Alexander Turner, and Aleksander Madry. 2018. Robustness may be at odds with accuracy. (2018).
- [64] Xiaosong Wang, Yifan Peng, Le Lu, Zhiyong Lu, Mohammadhadi Bagheri, and Ronald M Summers. 2017. Chestx-ray8: Hospital-scale chest x-ray database and benchmarks on weakly-supervised classification and localization of common thorax diseases. In *2017 IEEE Conference on Computer Vision and Pattern Recognition (CVPR)*. IEEE, 3462–3471.
- [65] Matthew K Wynn, Deborah S Cummins, Jonathan B VanGeest, and Ira B Wilson. 2000. Physician manipulation of reimbursement rules for patients: between a rock and a hard place. *Jama* 283, 14 (2000), 1858–1865.
- [66] Hongyi Zhang, Moustapha Cisse, Yann N Dauphin, and David Lopez-Paz. 2017. mixup: Beyond empirical risk minimization. *arXiv preprint arXiv:1710.09412* (2017).