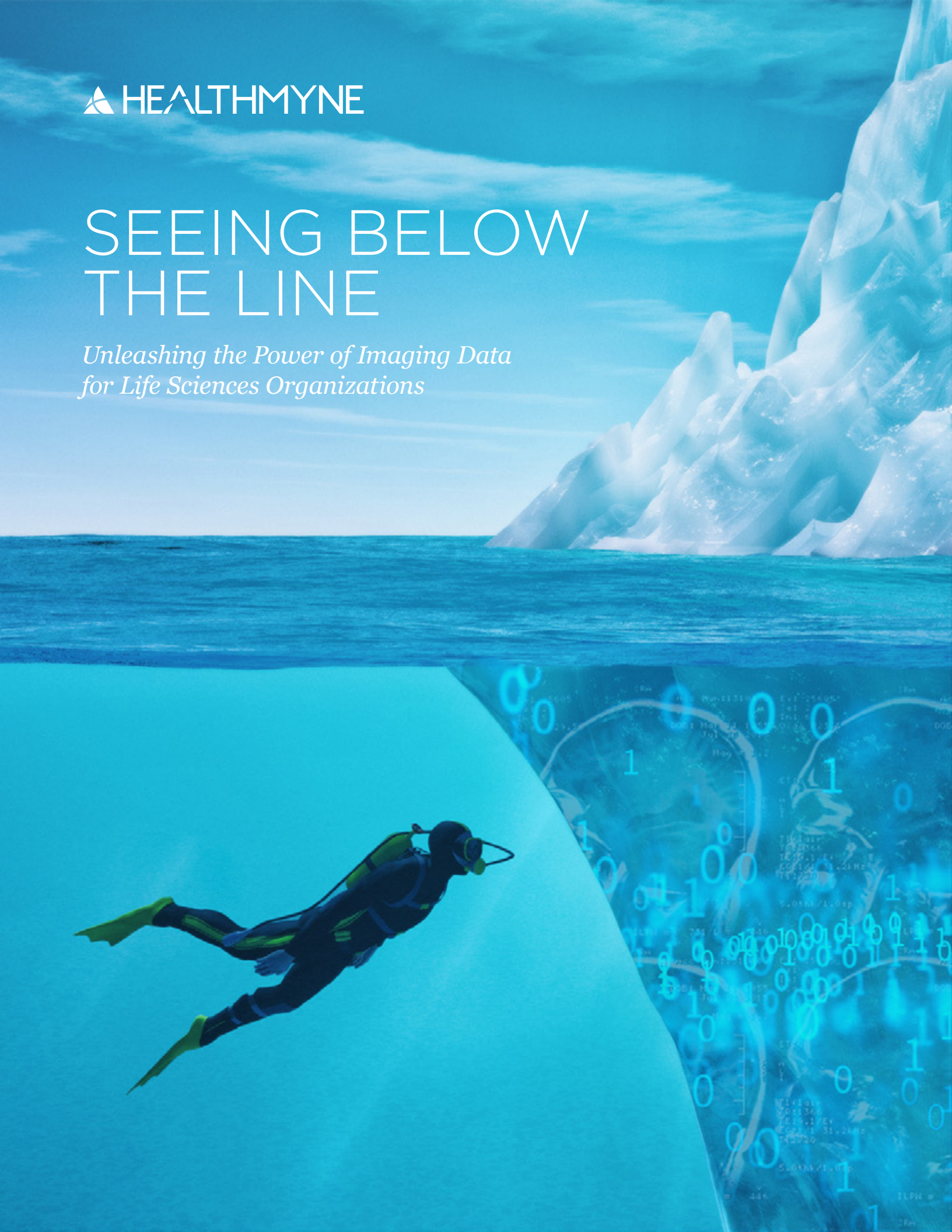
HEALTHMYNE

SEEING BELOW THE LINE

Unleashing the Power of Imaging Data for Life Sciences Organizations



Chapter 1

The Basics: Data That Gives Depth to Medical Images

When the term "big data" is used in healthcare and life sciences, there is often an assumption that these millions of petabytes of data are spread fairly evenly across many areas. Yet according to GE Healthcare, 90% of healthcare data is concentrated in one sector: medical imaging. And of that data, 97% goes unused or unanalyzed.

Traditionally, when clinical or research radiologists have received images of lesions or tumors to determine the effectiveness of a pharmaceutical or other treatment, their view has been limited to two dimensions – length and width (aka the long/short). As a result, their primary method of evaluation of the progress of that lesion is to use a pair of calipers across the vertical and horizontal axes to determine whether the lesion is growing or changing. That's like looking at a photo of an iceberg from the top.

The reality is lesions and tumors have multiple dimensions, along with thousands of other structural features that define them. Human cancers in particular exhibit strong structural (phenotypic) differences that can be visualized noninvasively by medical imaging. Gaining this view, however, requires seeing below the line.

That science of extracting the high-dimensional data from standard images to offer a comprehensive quantification of a lesion or tumor's phenotype is called radiomics. This relatively new approach extracts meaningful data from digital images, curates and annotates it, then analyzes the quantitative imaging data to deliver a wealth of information.

"Radiomics unleashes powerful insights about the characteristics and progress of lesions and tumors that are not discernible from traditional imaging..."

Radiomics unleashes powerful insights about the characteristics and progress of lesions and tumors that are not discernible from traditional imaging modalities such as CT, MRI, or PET scans so life sciences organizations can leverage them in new and exciting ways. Further, this novel set of imaging pattern data enables the discovery of imaging biomarkers which have been proven to be both predictive and prognostic regarding clinical outcomes and treatment pathways.

AI and deep learning-driven

The growth of artificial intelligence (AI) and deep learning (DL) technologies has made the application of these new insights into existing research and clinical workflows possible. These advanced techniques have accelerated and eased the ability to tap into multidimensional data no one has been able to use until now.

Radiomics at the foundation starts by building an AI-enabled model based on thousands of healthy organ images. The algorithms also ingest thousands of variations from that model that show lesions, tumors, their progress, and outcomes. As a result, rather than being limited to looking simply at length and width (long/short), AI-driven analytics can use this information to extract unseen data from the digital image to measure and determine depth, volume, density, doubling size, tumor textures and other features that cannot be observed optically in an image. These analytics not only deliver a view that formerly could only be achieved through invasive surgery such as biopsies; they also provide information about lesion changes that have never been available by any means.

Additionally, the DL capabilities inherent in HealthMyne's approach to radiomics enables the system to improve itself as more images are ingested and analyzed and more outcomes are confirmed –

regardless of the type of lesion. Over time, the system can track the progression or regression of lesions more accurately to determine the effectiveness of the treatment, providing new insights to life sciences organizations to leverage in therapeutic pipeline decisioning-such as accelerating or ending drug development based on treatment efficacy.

The more it learns the more the model can be fine-tuned and the more precise and individualized the insights become, taking us the next step closer to true personalized medicine.

Determining treatment effectiveness

Radiomics' ability to extract data from digital images and show what would otherwise be unseen can be used in multiple ways within life sciences organizations.

For example, it can help accelerate clinical trials by comparing sequential images to determine how a lesion has changed, indicating whether the drug is effective, why it is effective, to what degree it is effective, and how long it takes to achieve that effect. This information can be gathered in real time during the trial rather than waiting until it is completed (as typically occurs) to enable the life sciences organization to adapt the trial design based on radiomic features and imagining biomarkers. The result is that life sciences organizations can narrow the target population as the clinical trial moves from phase 2 to phase 3, eliminate barriers, and shave significant time off the process, reducing costs while helping to bring the right treatment to the right people faster. They can also determine more effectively when it's time to end a clinical trial that may not be performing.

"The combination of genomic data, plus the type of phenotypic data radiomics derives from images, will give even greater adaptability to clinical trials by immediately mapping the effectiveness of drugs, showing whether treatments under trial are more effective for patients with shared characteristics."

Another way radiomics can contribute value is in delivering the last mile in personalized medicine. The combination of genomic data, plus the type of phenotypic data radiomics derives from images, will give even greater adaptability to clinical trials by immediately mapping the effectiveness of drugs, showing whether treatments under trial are more effective for patients with shared characteristics. It will also inform whether a treatment or therapy is likely to be effective before a clinical trial starts, enabling life sciences organizations to focus their efforts where the likelihood of success is high – and ensure patients are not involved in trials or treatment course where they will experience no or minimal value.

In the long-term, radiomics can be used to discover imaging biomarkers to aid in clinical decision-making and treatment. Once they are developed, life sciences organizations can use these biomarkers to inform and manage patient recruitment, assignment to trial arms, and cohort design, such as inclusion criteria and stratification. They can also use them to inform phase advancement and even when a clinical trial should end rather than investing more in a dead-end product. Ultimately, imaging biomarkers' ability to predict therapeutic outcomes, and prognosticate on various "what-if?" scenarios, will deliver even greater precision in screening potential candidates for trials and delivering more individualized treatment plans.

In the following chapters we will look in greater detail at some of the vital ways radiomics can help life sciences organizations enhance and accelerate drug treatment development and the impact to commercial strategies.

Chapter 2

Accelerating the Pace and Cost-Effectiveness of Clinical Trials with Radiomics

Unlike many industries that create a product then look for a market, life sciences organizations are very methodical about first identifying a need for a specific drug before beginning the development process. This approach is largely driven by the economics of the process.

The Tufts Center for the Study of Drug Development estimates that the cost to bring a new drug to market is more than $2.8 billion. Other industry studies place the baseline at $1 billion, with costs for oncology and immunology-related therapeutics, which account for 90% of the spend, showing a median of $2.8 billion and a mean of $4.5 billion.

What these figures don't show is the low success rate that results from these efforts. The chances of a compound making it from development in a lab to even a Phase 1 trial are less than 10%. This fact places even greater pressure on those products that make it into a clinical trial to be successful.

Often, however, it takes a long time to determine the effectiveness of a particular treatment. Many drugs that show early promise in small-group trials ultimately fail because, while the indicators that a treatment doesn't have the efficacy for a broader application may be present, clinical researchers lack the means to observe the underlying structural evidence of response. As a result, life sciences organizations end up throwing good money after bad – a fact they don't realize until much later.

Radiomics drives earlier decision points

Radiomics solves this dilemma by analyzing medical imaging data to identify patterns linked to the structural (phenotypic) characteristics of tumor biology or diseased tissue. Prior to the advent of radiomics, this critical phenotype information would typically require a biopsy be performed to ascertain a single time specific snapshot of the lesion. In contrast to biopsies, medical imaging is usually noninvasive, can be applied longitudinally, and provides information about the entire tumor volume and underlying tumor characteristics. The radiomic features extracted from the image can be used to enable clinical research teams to inform whether a clinical trial should be continued, altered or halted much earlier in the process to help direct resources where they are most likely to yield an effective, viable product.

"The radiomic features extracted from the image can be used to enable clinical research teams to inform whether a clinical trial should be continued, altered or halted much earlier in the process to help direct resources where they are most likely to yield an effective, viable product."

Key to its effectiveness is radiomics' ability to enable research teams to compare sequential images across multiple dimensions and multiple timepoints. This comparison is used to determine what effects (if any) a drug in a clinical trial is having. Additionally, radiomics' ability to display the full history across those multiple dimensions on-demand offers a more in-depth view of whether the therapy is effective and how that effect has taken shape.

The result is that the technology goes well beyond the surface view of traditional imaging to deliver higher order statistics and the delta radiomics observed in them to help determine clinical endpoints. For example, heterogeneity is a critical element in oncologic progression. Radiomics can measure heterogeneity to discern the response to a particular treatment.

Armed with this information, project leaders can determine whether a trial has reached a clinical endpoint far more quickly than they can without radiomics They can also gain a better understanding of how the tumor or lesion is responding in the trial, allowing them to monitor and manage that trial more effectively..

Deeper layers of understanding

While the ability to make go/no-go decisions earlier is extremely valuable in helping life sciences organizations allocate their budgets where they have the best chance of success, that is not the only advantage radiomics offers in clinical trials history.

The information can also be used in adaptive clinical trials to make adjustments mid-trial that enable a promising but limited therapy to be tested more appropriately and thoroughly. Using the understanding gained to that point, life sciences organizations can risk-stratify their cohorts to eliminate those in the original group for whom the therapy is ineffective and add more individuals who may have originally been left out but may benefit after all.

On the other hand, where the therapy does show promise, radiomics can help clinical researchers understand why and how it was effective. What changes did it bring about? How quickly did it have an effect? To what degree was it successful?

Once all this information has been analyzed it can be applied to create more refined patient segmentation which can be applied to recruitment for new trials. This cycle of continuous refinement includes the future development of imaging biomarkers that can be used similarly to the way genomic biomarkers are used today, helping narrow the field to the patients most likely to receive the greatest benefits from a specific therapy based on the data. As more is learned about who is being affected by a drug, how and what to what degree, the radiomic features and imaging biomarkers will give clinical researchers the information they need to adapt the trial design to yield the best results.

Finally, these factors will also help identify candidates more precisely for critical Phase 4 clinical trials out of those who have already had success in previous phases.

"The data generated through radiomics can help keep clinical trials on-track and provide early warning of factors necessitating adaption of the trial based on new information."

Business benefits

Once a therapy has completed a clinical trial, the data generated through radiomics offers two key business benefits.

The first is the ability to bring the most effective drugs to market in the shortest possible time and at the lowest possible cost. The data generated through radiomics can help keep clinical trials on-track and provide early warning of factors necessitating adaption of the trial based on new information. It also provides additional data for review by government agencies attesting to the efficacy and safety of the therapy. Finally, it helps eliminate dead ends faster so resources can be redirected to where there is a greater chance for success.

"Much of the value of radiomics is its ability to bring precision to the treatment of various conditions and disease states."

The second is the ability to compare data from this therapy to positive and negative outcomes for other clinical trials and competitive products to help justify the cost of drugs to health plans. The more demonstrable and precise the results of a trial are, the more likely (and sooner) a health plan will be able to approve that drug for use and add it to its formulary. The specificity radiomic data brings will ensure the care itself is more personalized and effective, supporting value-based outcomes while informing payment and reimbursement strategies.

Much of the value of radiomics is its ability to bring precision to the treatment of various conditions and disease states. This orientation is in keeping with the move from a generic, one-size-fits-all approach to more individualized therapies. In the next chapter we will examine in greater detail how radiomics is enhancing the personalization of medical treatment.

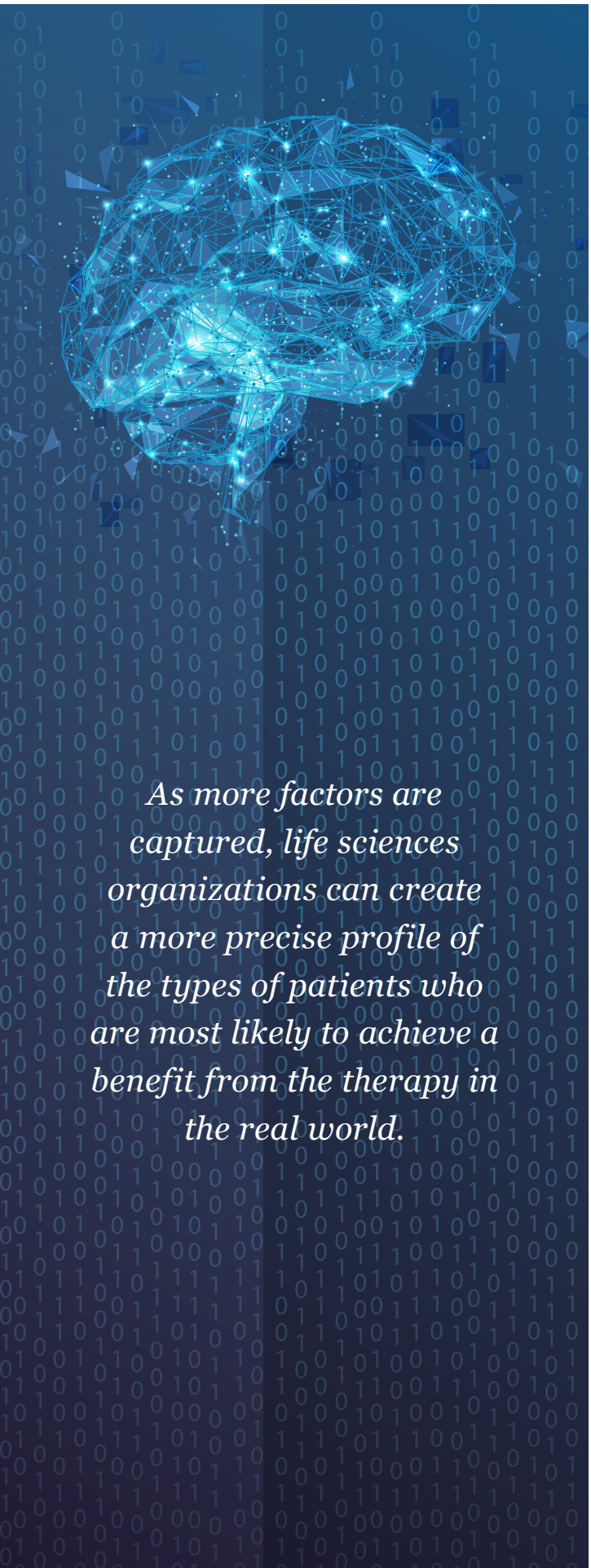
Chapter 3

Making Medicine Even More Personalized

Personalized medicine has been positioned as the next exponential improvement in healthcare. Advances in genomics have enabled treatments to move from broad, blanket approaches that varied in effectiveness to more precise therapies specifically targeted to an individual's genetic makeup. Radiomics offers the next chapter in this evolution to personalized care.

Historically, life sciences organizations waited until a clinical trial was completed before gathering and analyzing data. That approach has been changing in recent years. The introduction of adaptive clinical trials has resulted in reviews and analyses being performed throughout the process. If relevant data from laboratory work, imaging, or other sources presents itself, the trial can be adapted (with FDA approval) to account for these factors. The more data that is captured and analyzed as the clinical trial proceeds, the more precise and accurate the conclusions of the trial will be.

Radiomic data is a highly valuable addition to this dataset. By showing previously hidden trends within a lesion or tumor, Radiomics can be an early indicator of the effectiveness of the treatment.



As more factors are captured, life sciences organizations can create a more precise profile of the types of patients who are most likely to achieve a benefit from the therapy in the real world.

Radiomic data is a highly valuable addition to this dataset. By showing previously hidden trends within a lesion or tumor, Radiomics can be an early indicator of the effectiveness of the treatment. And by bringing to light the tumor phenotype (structural characteristics) radiomics helps address disease progression, metastatic potential, and response to therapy.

By using artificial intelligence (AI) to discern and compute data from medical images, life sciences organizations can profile the patient, the tumor and the therapy across multiple dimensions to find patterns and similarities that would otherwise require a huge expenditure of time and resources. As more factors are captured, life sciences organizations can create a more precise profile of the types of patients who are most likely to achieve a benefit from the therapy in the real world.

On a broader scale, introducing radiomic data into adaptive clinical trials may speed up or shorten the trial by giving it greater focus. If researchers realize early in the trial the characteristics shared by those for whom a therapy is most effective, they can concentrate their efforts there. Life sciences organizations can also determine if the market for a particular drug that appears to benefit only a small subsegment of the target population is significant enough to continue pursuing.

Improving Phase 3 outcomes

One area where the deeper results of radiomics is particularly beneficial is when Phase 2 of a clinical trial is about to move into Phase 3. This is where the greatest risk of wasted time and investment lies.

With radiomics, researchers can gain a greater understanding of the characteristics shared by those for whom the treatment has been most effective, and those for whom it has had little to no effect. They can then

recruit more patients who share the targeted characteristics to see if there are even deeper similarities, or there are any barriers within what appears to be the target group that would prevent success.

With this greater focus, life sciences organizations can shave a significant amount of time off a 10-year trial process, substantially reducing costs while bringing the most optimal treatments to every patient every time.

Justifying costs to health plans

While the benefits of personalized medicine are mostly focused on the health outcomes, the data generated by radiomics are also valuable in justifying the cost of a particular therapy – especially one that costs appreciably more than a competitive product – to health plans.

Imaging biomarkers generated through radiomics add to the clinical evidence supporting the effectiveness of a particular therapy. Rather than being a "one-size-fits-all (sort of)" approach, data acquired through radiomics enables life sciences organizations to quantify how much more effective their new product is for a set or subset of patients with a given condition.

This apples-to-apples comparison can be linked to economic projections to show why a larger investment now will pay greater dividends over the lifetime of a member, framing the discussion in terms of value-based care. Life sciences organizations may also be able to demonstrate that the faster and more certain improvements generated by the new therapy are likely to shorten the amount of time spent in treatment, reducing the overall investment (including ancillary costs).

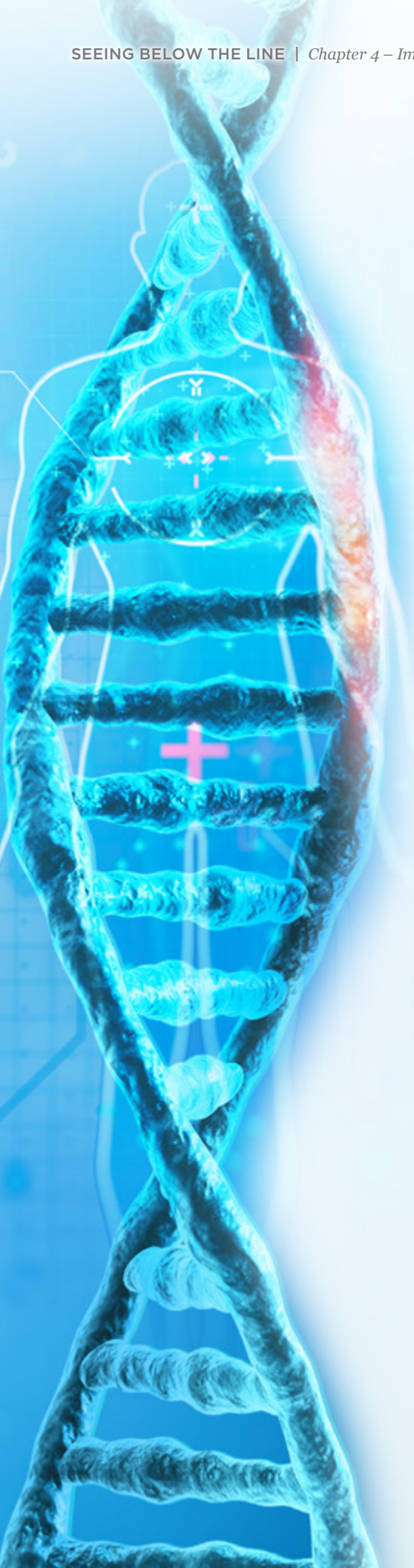
Rather than being a "one-size-fits-all (sort of)" approach, data acquired through radiomics enables life sciences organizations to quantify how much more effective their new product is for a set or subset of patients with a given condition.

A higher likelihood of success versus competitive products also means the member lives a longer life in greater health, which directly translates to more long-term revenue.

The bottom line is that with the additional data generated by radiomics measurements, health plans receive greater assurance that their members who fit the appropriate treatment protocol and profile are most likely to achieve their best possible health outcomes. Additionally, life sciences organizations will have the data they need to create additional justifications and selling points in the future.

All of what has been discussed in this Ebook so far are benefits that can be achieved within the scope of radiomics today. Perhaps the greatest promise, however, lies in the future with the potential development of imaging biomarkers that will inform clinical decision-making in the future.

This apples-to-apples comparison can be linked to economic projections to show why a larger investment now will pay greater dividends over the lifetime of a member, framing the discussion in terms of value-based care.



Chapter 4

Improving Clinical Decision-Making through Imaging Biomarkers

In the previous chapter we looked at how radiomics is enhancing personalized medicine today. The ability to read multiple dimensions in a lesion to determine how it is reacting to a treatment, and to use artificial intelligence and analytics to categorize those reactions, is helping guide clinical researchers to more precise conclusions.

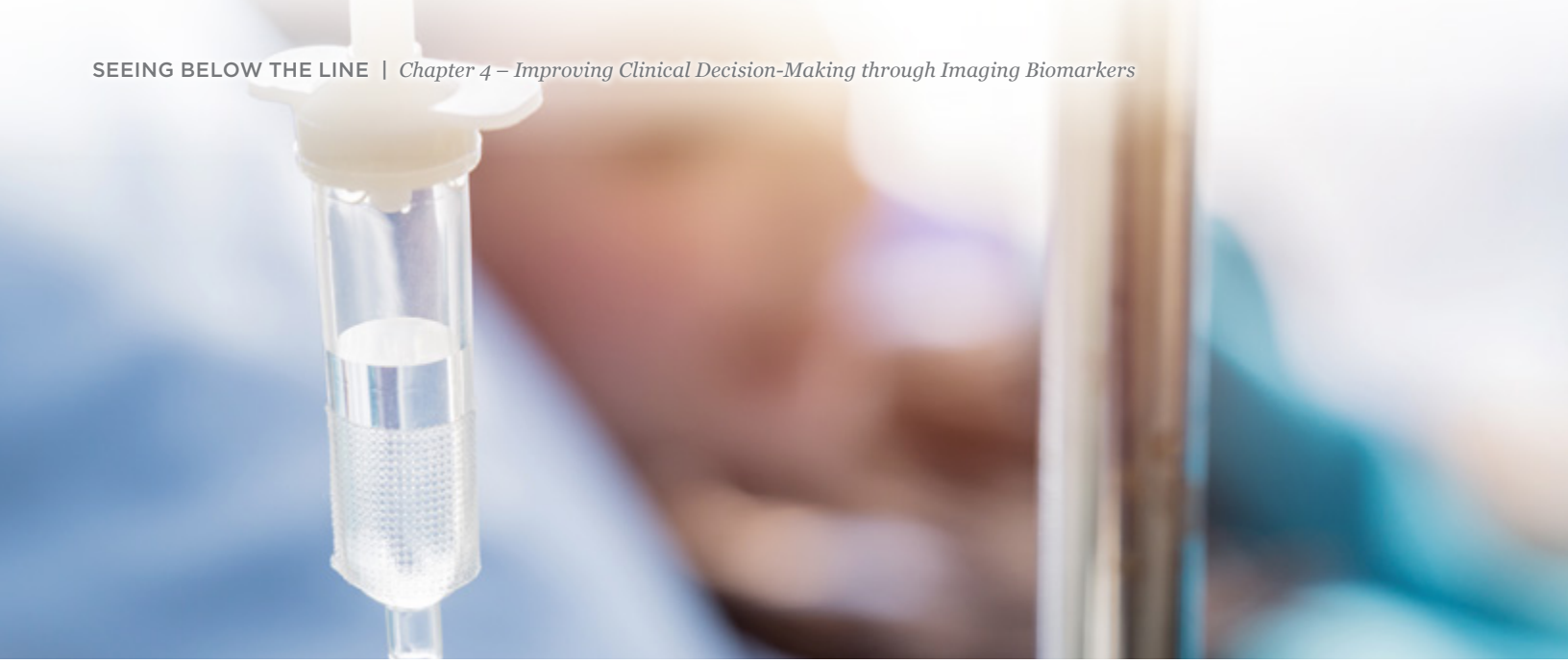
There is another level on the horizon, however – one that will enable more predictive and prognostic analyses: the development of imaging biomarkers.

Preemptive identification of issues

The theory that medicine could be more precisely personalized based on an individual's biologics has been proposed for several decades. It wasn't until the first genetic map was developed in 1987, however, that it went from theoretical to practical application.

In the ensuing years, scientists have been able to identify genetic biomarkers that predict certain health conditions, such as an individual's likelihood of developing specific types of breast cancer. These biomarkers not only help frontline clinicians improve patient care and take preventive measures but also help life sciences organizations find the research study candidates who are most predisposed to success when given a particular therapy.

By narrowing the field from the beginning to the most likely beneficiaries, life sciences organizations can save time in the early stages and get to Phase 3 with higher prospects of success. They are now in the process of educating providers about this advancement.



The quest for imaging biomarkers

This same principle is now in its early stages in radiomics. Private industry is working with academia to develop imaging biomarkers derived from radiomics that will add another layer to the personalization of medicine.

Using the radiomics data that has been and continues to be accumulated, along with AI-driven analytics, researchers in this area are digging below individual events to understand what is happening in the cellular structure of healthy organs and those with lesions. There are two goals for this research.

The first is to identify the imaging biomarkers that can predict how a patient will respond to a specific treatment. This alone is a monumental challenge, made more difficult by the uncertainty of success.

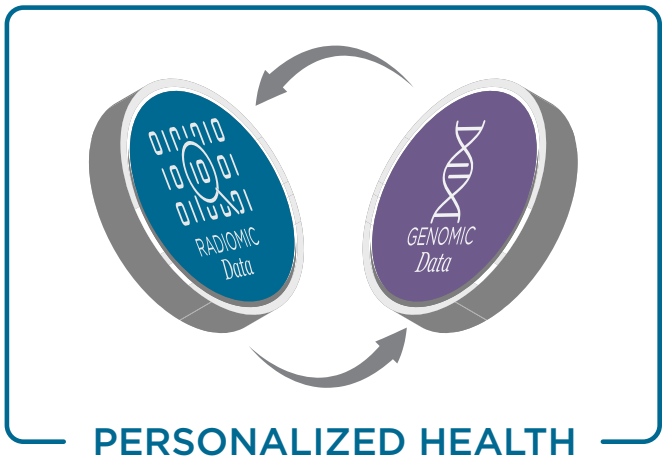
With genetic biomarkers, once the human genome was mapped and understood more fully, it was clear that there were differences that had a high likelihood of correlating to specific disease conditions. Although discovering the relationships was challenging, it was clear they existed.

With imaging biomarkers, the path to success is less certain. There is no overall genetic code that can be used as a Rosetta Stone to unlock the mysteries. Everything about imaging biomarkers must be developed from raw data.

The second goal is to offer real-world imaging evidence that the predictions and outcomes are directly tied to specific biomarkers. Once the imaging biomarkers have been identified in theory, more analytics will be required to ensure that the perceived relationship is true in all cases rather than coincidental or valid only under certain conditions.

Getting to that point will require a great deal of effort. But if successful, it will be worth it. Because where genetic biomarkers offer the starting point for personalization, i.e., these patients are more genetically predisposed to success than others, imaging biomarkers demonstrate whether the treatment that was recommended is generating (or is likely to generate) the desired results.

Radiomic Data



Genomic Data

The use of both genomic and imaging biomarkers is expected to have a substantial, positive impact on the way clinical trials are constructed and managed. The combination of the two will significantly narrow which patients are selected to receive a specific treatment, saving time and money at each stage. It will also help life sciences organizations justify higher prices for their therapies in the field because they will have more robust evidence that use of those therapies with the patient exhibiting the appropriate genetic and imaging biomarkers will produce the desired health outcomes.

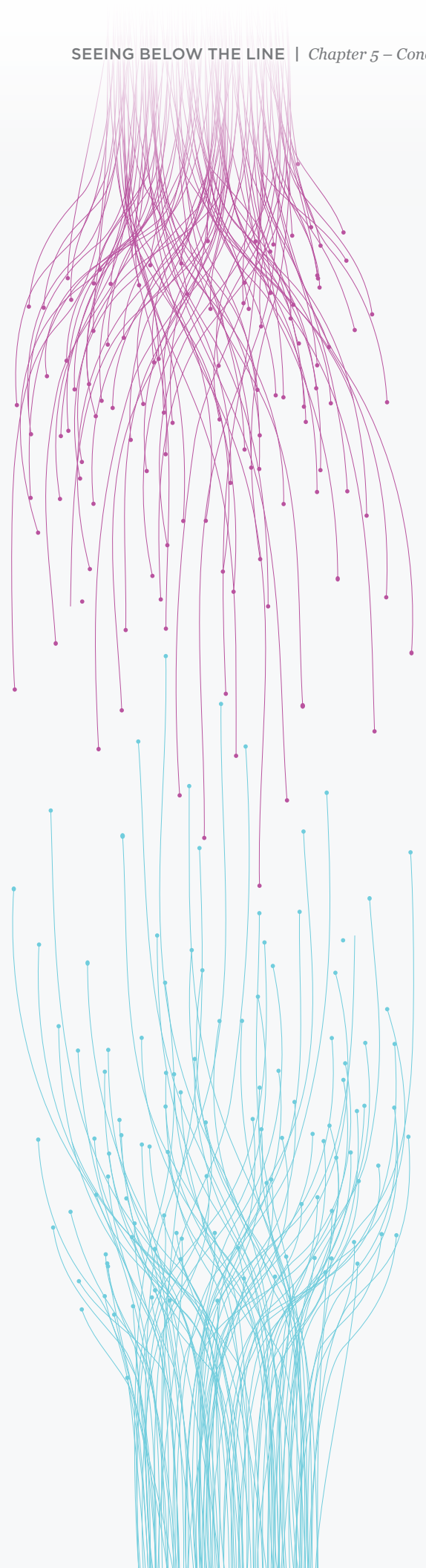
"...imaging biomarkers demonstrate whether the treatment that was recommended is generating (or is likely to generate) the desired results."

Still early

While radiomics has given researchers the tools required to discover imaging biomarkers, the number and applicability of their use continues to be studied. The growing body of evidence strongly suggests a promising future for imaging biomarker discovery and adoption across the healthcare continuum.

For many diseases, and cancer in particular, early intervention is critical to achieving healthy outcomes. The use of genomic and imaging biomarkers together will help ensure that the right intervention is being applied as soon as the issue is identified, improving the chances for success – and survival.

"The use of genomic and imaging biomarkers together will help ensure that the right intervention is being applied as soon as the issue is identified, improving the chances for success – and survival."



Chapter 5

Conclusion

High-quality imaging is crucial to understanding the effectiveness of therapies, whether in clinical trials or actual patient care. Yet traditional images, even those taken with the most sophisticated equipment, still only offer a very limited view of changes in a tumor or lesion.

Often those images can be misleading, either missing growth outside their two-dimensional view or causing concern where it is not needed. When that occurs, it leads to less-than-optimal decision-making, such as continuing a clinical trial that should be concluded or an inability to focus on the patients for whom the therapy will be most effective.

Radiomics offers the ability to completely change how life sciences organizations can be informed by medical imaging. By using data and artificial intelligence to look below the surface to discern first through higher order metrics, it gives research teams greater ability to understand relevant changes that might otherwise be missed. While providing more precise information on which to base conclusions, it also reduces the risk of variation in reader interpretations. Thus, providing the ability to avoid costly missteps, such as knowing when to adjust course in a clinical trial, while reducing the time required to complete those trials.

Finally, radiomics offers the opportunity to develop imaging biomarkers that will enhance personalized medicine by working in conjunction with genomic biomarkers. The genomics will identify the patients most likely to develop a particular condition while the radiomics will use structural or phenotypic data analysis, proving new insights in calculating the potential success of various therapeutics to address that condition. Together they will help bring new therapies to market faster as well as ensuring the right therapies get to the right patients at the right time.

Radiomics promises to be one of the most exciting developments in the successful treatment of a variety of conditions, including cancer, in the last 50 years. It is well worth delving below the line to see all the benefits radiomics offers to life sciences organizations.

HEALTHMYNE®

918 Deming Way, Madison, WI | HealthMyne.com | Info@HealthMyne.com