Quarks, Leptons, Fermions, Bosons:

The Subatomic Pharmacology of Radiation Therapy

James S. Welsh

Modern radiology techniques have achieved widespread use and impressive results in cancer diagnosis and treatment. Yet, the nature of the subatomic particles used in the "rays" in these techniques remains unclear to many clinicians. High-energy photons, including x-rays and γ-rays, are bosons, whereas electrons and positrons, used in PET, are leptons. Less often used are protons and neutrons, which are composed of quarks and classified as hadrons. This article reviews the subatomic world of particle physics and the elementary forces that interact with these particles, and explores how these particles and forces are employed in modern radiologic technologies.

Sci & Med 10(2):124-136, 2005.

Publication date: 10 Nov 2005

Modern radiation therapy is an important component of management of many patients diagnosed with cancer. Every year, over a million patients are treated with radiation therapy for malignant disease, with about 75% treated with curative intent and 25% for palliative purposes. Despite the widespread use, impressive results, and fascinating technology used in modern radiotherapy, many physicians remain relatively naïve about the basic "pharmacology" of the radiation prescribed in the efforts to fight and diagnose disease.

For example, the high-energy photons (i.e., x-rays and γ-rays), so valuable in diagnosing and treating cancer, are *bosons* based on their quantum spin. Electrons are invaluable in the treatment of many malignant and benign conditions, and their antimatter counterparts, positrons, are becoming increasingly more important in diagnostic imaging with positron emission tomography (PET). Electrons and positrons are *leptons*, as they do not interact via the so-called strong nuclear force. On the other hand, protons and neutrons (and the quarks they are made of) do interact via the strong force and therefore are *hadrons*.

This article provides a brief overview of the various particles used in radiation therapy and explains where they fit in the subatomic world. The story begins with a look at the early radiation research that presaged the medical applications.

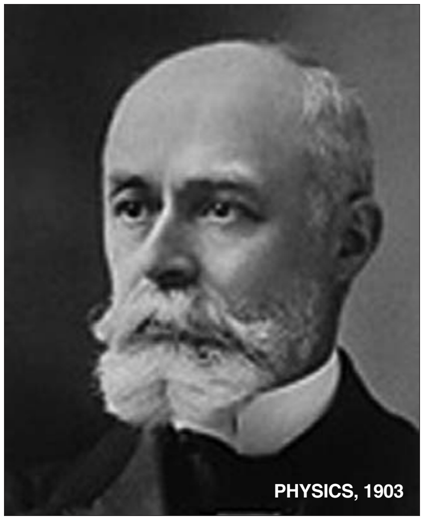
Early Research Led Quickly to Medical Applications

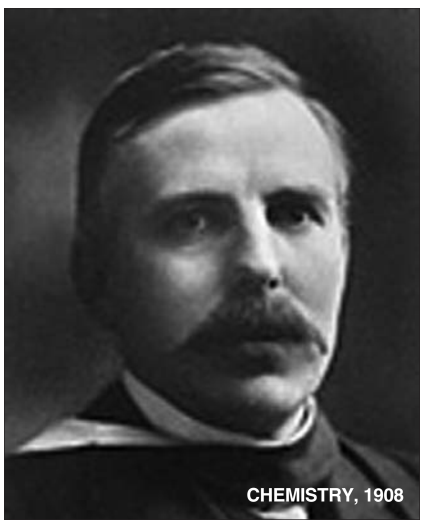
On 8 November 1895, while investigating "cathode rays" (i.e., electrons) at the University of Wurzburg, Wilhelm Roentgen noticed a curious glow on a fluorescent screen on a nearby table. Roentgen immediately recognized that the fluorescence was caused by invisible rays emanating from the partially evacuated glass Hittorf-Crookes tube he was using. He also realized that these mysterious rays penetrated the opaque black paper wrapped around the tube.

Roentgen had discovered x-rays, a momentous event that instantly and permanently affected the fields of physics and medicine. For this discovery, Roentgen received the first Nobel Prize in physics in 1901.

Only months after Roentgen's discovery, Henri Becquerel was experimenting with potassium uranyl sulfate, in which he exposed the material to sunlight and then placed it on photographic plates wrapped in opaque black paper. The plates revealed images of the uranium crystals upon developing. Becquerel concluded that "the phosphorescent substance in question emits radiation which penetrates paper opaque to light."

He initially assumed that solar energy was absorbed by the uranium, which then emitted x-rays. However, during a few cloudy days in Paris, he put his work aside (literally) and set the plates in a draw-





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Five early pioneers in basic radiation research received Nobel prizes (*from top left*): Wilhelm Roentgen, Henri Becquerel, Marie and Pierre Curie, and Ernest Rutherford. Their contributions paved the way for the many clinical applications of radiation.

er. When he exposed the plates about a week later, he expected to observe only a faint image. To his bewilderment, the images were strong and bright.

Becquerel realized the uranium itself was emitting a new form of radiation. In contrast to Roentgen's x-rays, the radiation emitted by the uranium samples could be deflected by a magnetic field, implying that it consisted of a stream of charged particles. Becquerel was awarded the 1903 Nobel Prize in physics for his discovery of what later became known as radioactivity.

The term *radioactivity* actually was coined by Marie Curie, who together with her husband Pierre, further investigated Becquerel's discovery. Working in primitive conditions (using an alley and shed as research facilities), the Curies extracted uranium from ore and were astonished when the leftover ore actually showed more radioactivity than the purified uranium. They concluded that the ore contained other radioactive elements,

Early Medical Applications of X-rays

Medical applications of x-rays and radioactivity emerged very shortly after their discovery.

- Emil Grubbe, a Chicago electrician and metallurgist, treated a recurrent breast cancer in a 55-year-old woman in January 1896, only weeks after Roentgen's discovery was announced. Grubbe did not publish his work until several years later, and his claim to be the first to use radiation treatment for cancer remains controversial.
- In 1898, Chicago dermatologist William Pusey reported beneficial effects of x-rays for hypertrichosis and acne, while Leopold Freund in Vienna, pioneered the use of x-rays in certain other benign conditions.
- In 1899, in Stockholm, Thor Stenbeck initiated a 9-month treatment for a 49-year-old woman with basal cell skin cancer of the nose; the patient was reported to be alive and well 30 years later.
- Also in 1899, Tage Sjörgen began effective treatment of a patient with squamous cell skin cancer, using 50 treatments given over 30 months.
- In 1901 in Boston, Frands Williams used x-rays to cure a patient with a cancer of the lower lip.
- In 1903, New York physician Margaret Cleaves speculated that radium might "prove a veritable Aladdin's lamp to medical science" and pioneered the field of gynecologic brachytherapy through the use of radium for patients with cervical cancer.

See the paper by James Welsh and Christine Berta on "Radioimmunotherapy for Disseminated Lymphoma" in the September/October 2002 issue of Science & Medicine (page 246).

eventually leading to the discoveries of polonium and radium.

Ernest Rutherford, considered the father of nuclear physics by many, coined much of the terminology used to describe the atom and radioactivity. In his studies of radioactive decay, he named the emitted radiations *alpha*, *beta*, or *gamma* based on their ability to penetrate matter.

In 1909, Rutherford was bombarding a thin gold foil with α-particles when he noticed that about one in 8000 would "bounce back." Rutherford commented that it was "as if you fired a 15-inch naval shell at a piece of tissue paper and the shell came right back and hit you."

From this, Rutherford concluded that the mass of an atom must be concentrated in a dense, positively charged nucleus, while the light, negatively charged electrons orbited the periphery. Although this planetary model of the atom has been refined greatly over the years, it remains essentially correct.

Medical applications of x-rays and radioactivity emerged shortly after these discoveries, and from modest beginnings, the field has evolved into a complicated discipline involving some of the most sophisticated technology in medicine.

External beam radiation therapy began with simple x-ray tubes. It was observed that as x-ray photon energy increased, the depth of penetration of the clinically useful radiation dose improved and skin side effects decreased.

As technology improved, therapeutic x-ray photon energies increased from tens of kilo-electron volts (keV) to hundreds of keV. Because even higher energy γ-rays (1.17 and 1.33 million electron volts, MeV) emanated from cobalt-60, teletherapy units were developed using this isotope and were first used to treat cancer in the early 1950s.

These units were succeeded by medical linear accelerators capable of generating photon beams of even higher energies. Currently available linear accelerators regularly deliver radiation therapy using photon beams with energies of tens of MeV.

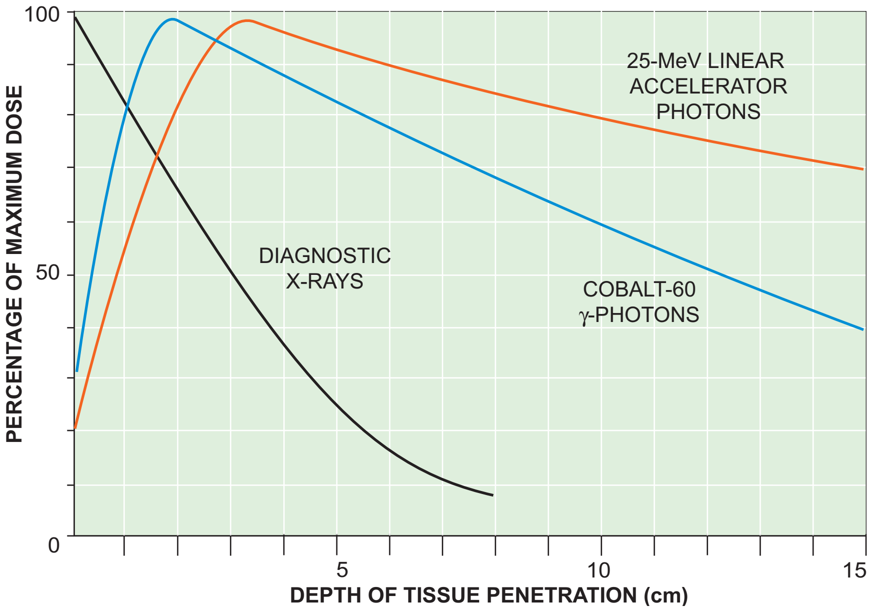
Modern external beam radiation therapy is administered via high-energy linear accelerators that are often capable of producing both photons and electron beams, which have specific clinical applications. When used with shaped blocks, these beams can be customized to match the specific anatomy of the target.

Many linear accelerators now are capable of more sophisticated techniques of modifying photon beams, such as intensity-modulated radiation therapy (IMRT) and 3-dimensional conformal radiation, which greatly improve the ability of clinicians to deliver high doses of radiation to targeted areas while simultaneously reducing the dose to sensitive structures. Proton beams have some intrinsic dosimetric advantages over photons and electrons that allow extremely effective targeting and sparing of normal tissue. Several cyclotrons have been designed specifically for proton therapy, and more are under construction.

Brachytherapy techniques unheard of a few decades ago are now commonly used to treat prostate and other cancers. For instance, radioactive "seeds" containing iodine-125 or palladium-103 have become a popular choice for the treatment of early-stage prostate cancer.

Radioimmunotherapy, the use of radioactively tagged antibodies, is emerging as a clinically valuable weapon against non-Hodgkin's lymphoma and is being investigated for other applications.

While the technology of modern radiotherapy is impressive, the elementary fundamentals of the various forms of radiation routinely prescribed to fight and diagnose disease remain a fascinating subject that is often underappreciated by many clinicians, even those who routinely prescribe it.



The depth of penetration of a radiation dose varies as a function of photon energy. In general, with higher energy photons, there is less dose deposited in skin and greater penetration at depth.

Protons and Neutrons Are Composed of Quarks

High-energy x-rays and electrons are the most commonly prescribed types of radiation in external beam radiation therapy, but a few facilities are also capable of irradiation with protons or neutrons. Brachytherapy, in which radioactive isotopes are placed in direct proximity to the tumor, either permanently or temporarily, uses primarily γ-rays and β-particles, and to a lesser extent α-radiation.

Just what are these various forms of radiation? To start, we briefly discuss the basic building block of chemical importance, the atom.

From a chemical point of view, the properties of an element are reflected by the electron cloud surrounding its nucleus. An element's atomic number is given by the total number of protons, while its mass number is the total of protons plus neutrons.

It was initially believed that the atom nucleus was composed of exclusively protons and neutrons and that these so-called nucleons were indivisible basic building blocks of matter. It is now appreciated that nucleons are not indivisible units but rather are composed of still smaller particles known as *quarks*.

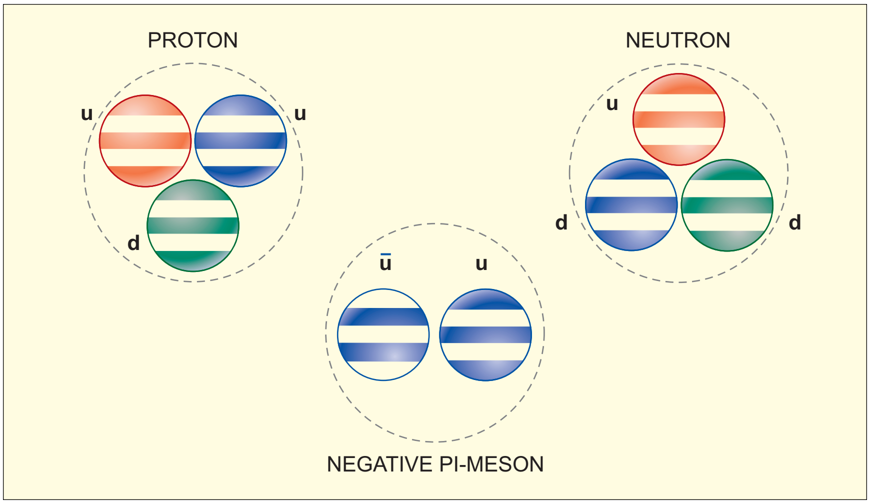
Quarks come in six "flavors," which go by the whimsical names of *up, down, strange, charmed, bottom,* and *top,* arranged in order of mass from lightest to heaviest. The two most massive quarks, bottom and top, are also occasionally referred to as *beauty* and *truth*. Based

Quarks and their Charges and Masses

Generation (Family)	Name	Symbol	Charge	Mass (MeV)
I	Up	u	+2/3	~5
	Down	d	-1/3	~7
II	Strange	s	-1/3	~150
	Charmed	c	+2/3	1500
III	Bottom (beauty)	b	-1/3	5000
	Top (truth)	t	+2/3	>41 000

Quarks come in six flavors, grouped into three generations. Each quark also can exist in three "colors": red, blue, and green. Quarks possess fractional charges.

Masses listed are "rest" masses. The astute reader might observe that the sum of the masses of the quarks that make up the proton, for example, are far less than the rest mass of the proton itself (938 MeV). This is because the mass of the composite particle is due mainly to the kinetic energy of the constituent quarks and gluons, rather than their summed rest masses.



Protons, neutrons, and the negative pion are composed of different colored quarks. All composite hadrons are colorless, because the constituent quark colors "cancel" each other out; thus, baryons are composed of three quarks of different colors (red, green, and blue together cancel), and mesons, like the pion, are composed of a colored quark and antiquark which cancel each other.

on properties such as charge, the six flavors of quarks are grouped into three families or generations: up and down, charmed and strange, and bottom and top.

The proton is made up of two *up* quarks and one *down* quark, while the neutron is composed of one *up* and two *down* quarks.

Knowing the net charges of the protons and neutron (+1 and 0, respectively) and that these are both composed of three quarks, one can see that quarks have fractional charges. The proton, with its net charge of +1 is composed of two *up* quarks each with a charge of +2/3 and one *down* quark with a –1/3 charge. The neutron, with no net electrical charge, is composed of two *down* quarks each with a –1/3 charge and an *up* quark with a +2/3 charge, canceling out to a net of zero.

Early Categorization Schemes Intended to Organize Particles

Long before physicists developed the quark model, a virtual zoo of unanticipated subatomic particles was emerging, identified through cloud chamber analyses of cosmic rays (high-energy charged particles from outer space). The early investigations of cosmic rays in the 1930s and 40s heralded the dawn of a new scientific discipline, elementary particle physics.

Further research in this new field required new technology, and thus high-energy linear accelerators, cyclotrons, and synchrotrons were devised. In the first experiments, energetic particle beams struck a stationary target, and the products generated from the collision were studied. Later, to maximize the energy of the impacts, particle beams were collided head-on at ever more powerful research accelerators.

Thus, in addition to the familiar protons and neutrons, exotic particles such as the muon, pi-meson, k-meson, delta, and sigma, among dozens of others, were discovered and added to the list of elementary building blocks of nature.

Categorization schemes were desperately needed to make sense of this expanding array of particles.

One initial classification scheme relied on the fact that many of these particles are unstable, decaying into daughter products very rapidly after forming. Regardless of whether these unstable particles breakdown quickly or slowly, they eventually lead to some collection of stable end products.

One such classification of particles was based on whether the final breakdown products included a proton. Particles that do include a proton as a final daughter product were called *baryons* (from the Greek word for heavy—the same root as in the term bariatric medicine). The proton itself is included in this class along with the neutron, lambda, sigma, delta, and numerous other particles.

Another means of classifying particles considered their mass. Particles with masses between that of the electron and proton (about 1836 times that of the electron) were called meso-trons, later shortened to *mesons*.

Thus, the *pi-meson* or *pion*, with a mass 273 times that of the electron, was classed as a meson. The *mu-meson* or *muon*, with its mass of 207 times that of the electron, also fit this definition and thus initially was considered a meson.

Numerous other particles of intermediate mass were discovered including the *k-meson* or *kaon*, but with greater understanding, a categorization based simply on mass proved inadequate and had to be revised when the quark model came into being. For instance, muons have numerous features that differ dramatically from other mesons, and they are no longer grouped with the mesons.

Another means of classifying particles relied on their participation in certain interactions or forces. Everything with mass is subject to gravitational force, and all electrically charged matter is subject to electromagnetic force. Yet, the so-called strong nuclear force, which holds the nucleus together, does not affect all particles; those that are affected are known as *hadrons* (from the Greek root for strong). Protons, neutrons, and all other baryons are considered hadrons, as are pions and all true mesons.

Particles not subject to the strong force, such as electrons and muons, are termed *leptons* (derived from the Greek word for small or light—the same root as used in the term leptomeningeal).

A later proposed categorization scheme was in many ways analogous to the periodic table of elements. In the periodic table, Dmitri Mendeleev discovered that as the chemical elements were arranged in rows (with increasing atomic number from left to right), natural groups formed such that the elements in vertical columns shared similar chemical properties.

In a similar fashion, the proliferation of hadrons could be plotted so that they formed natural groups with similar properties. When such a plot is created for the low-mass baryons, a logical and symmetrical pattern emerges with a set of eight particles. Because of the octet pattern, this scheme was dubbed the eightfold way.

Mendeleev's periodic table established its value by predicting the existence of the previously unknown elements germanium and scandium based on gaps in the table. In a similar way, the eightfold way proved its merit by predicting the existence of an unknown particle with certain expected characteristics. This particle, the *omega minus* (Ω^-), was eventually discovered, and its properties nicely matched those predicted by the eightfold way plot.

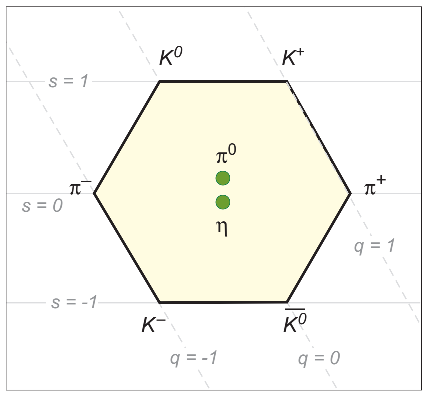
However, as with the periodic table, the eightfold way provided a plot that arranged particles in a logical pattern and predicted undiscovered particles, but it also provided little understanding of the basic nature of the particles or explanation of why such natural groupings should occur. The true significance of the periodic table was appreciated after the foundation of quantum chemistry and an understanding of valence electrons. Similarly, the eightfold way made more sense only after the quark model was formulated.

The Quark Model Redefines Hadrons, Baryons, and Mesons

With the advent of the quark model, a better understanding of hadrons became possible. As mentioned, hadrons are particles that interact via the strong force and include baryons (such as protons and neu-

Forces Affecting Subatomic Particles

Force	Affects
Gravity	Anything with mass
Electro-magnetism	Anything with charge
Strong nuclear	Quarks Protons Neutrons
Weak	All fundamental particles



The eightfold way octet for the lightest mesons. Particles along the same horizontal line share the same strangeness (*s*), while those on the same diagonal share the same charge (*q*).

Fundamental Particles in the Standard Model

LEPTONS		HADRONS		BOSONS	
Particle	**Symbol**	**Particle**	**Symbol**	**Particle**	**Symbol**
Electron	e^-	Baryons		Photon	γ
Muon	μ^-	Proton	p^+	Weak bosons	
Tauon	τ^-	Neutron	n^0		W^+
Neutrino	υ_e	Mesons			W^-
	υ_μ	Pion (pi-meson)	π^+, π^-		Z^0
	υ_τ		π^0	Gluon	g
		Kaon (k-meson)	K^+, K^-	Graviton (proposed)	
			K^0	Higgs (proposed)	
		Eta	η^0		

Spin varies among the groups: leptons, spin = 1/2; baryons, spin = 1/2; mesons, spin = 0; bosons, spin = 1.

trons) and mesons (such as pions and kaons), whereas particles not subject to the strong force are leptons.

In the quark model, mesons are defined as those hadrons made up of a quark/anti-quark pair. In this way, the pion remained a meson but the muon, which proved not susceptible to the strong force and not made of quarks, lost its status as a meson and was classed as a lepton.

With this newer definition, some particles of greater mass than the proton (e.g., the A_2 meson) could be considered true mesons if they are composed of a quark/anti-quark pair, despite not having an "intermediate" mass.

In a similar fashion, the quark theory provided a new definition of baryons—i.e., hadrons composed of three quarks. Thus, the hadrons, elementary particles subject to the strong nuclear interaction and composed of quarks, are now classified as baryons if they are made of three quarks and as mesons if they consist of a quark/anti-quark pair.

The Leptons Include Electrons and Other Particles

The muon, although intermediate in mass, did not share many characteristics with other mesons with which it was grouped in the older schemes. It is not subject to the strong nuclear force and is not composed of quarks. It does share many fundamental properties with electrons, however.

The electron is an elementary building block of matter not subject to the strong nuclear force, and therefore it belongs to the lepton family of particles. The same holds for its antimatter counterpart, the positron. Muons are now grouped with electrons as leptons also.

In addition, another lepton became known as the *tauon*. With a mass of about 3500 times that of the electron (roughly twice that of the proton), it was not small or light, as the term *lepton* originally implied. Like all other leptons however, tauons are not made of quarks and do not participate in the strong nuclear interaction.

Leptons do participate in the weak interaction, which governs phenomena such as radioactive decay.

Laws of physics, such as the conservation of electrical charge, momentum, and energy, are among the most basic of scientific principles, having withstood the tests of time and experimental challenge over and over. Thus, the initial studies of radioactive β decay were of major concern when the laws of conservation of energy and momentum appeared violated.

β–particles are leptons—either negatively charged electrons (β^-) or positively charged positrons (β^+). Unlike γ-ray or α-particle emission, however, the emitted β-radiation

The Leptons and Their Properties

Name (Flavor)	Symbol	Charge	Mass (MeV)
Electron	e^-	-1	0.511
Electron neutrino	υ_e	0	0*
Muon	μ^-	-1	105.7
Muon neutrino	υ_μ	0	0*
Tauon	τ^-	-1	1784
Tau neutrino	υ_τ	0	<35

* There is evidence that these neutrinos are not actually massless.

does not always have a discrete energy, just a maximum limit. A β-particle can have any energy, ranging from zero to a maximum value characteristic of a specific radioisotope.

On average, the kinetic energy of an observed β-particle is only about one third the energy difference between the parent and daughter products. As this appeared to violate the conservation of energy and momentum, the options were either to abandon these laws or to propose the radical idea that another unnoticed particle accompanied the emitted β-particle that would conserve the energy and momentum.

Wolfgang Pauli in 1930 first conjectured the existence of a second particle emitted simultaneously with the β-particle that carried the "missing" energy and momentum. Enrico Fermi further elaborated this hypothesis, proposing an electrically neutral, massless particle with almost no tendency to interact with matter, which he named the neutrino.

At first, the idea was scoffed at, but on further scrutiny, it was found that the proposed particle would conserve not only energy and momentum but also angular momentum (spin) and another property, lepton number. A particle capable of preserving four important laws of nature became far more plausible, and an active search for the particle ensued.

In 1956, 26 years after Pauli's initial proposal, Reines and Cowan announced the detection of the neutrino (actually an anti-neutrino). The neutrino it turns out is another lepton and comes in three basic varieties, one for each of the other leptons: an electron neutrino, a muon neutrino, and a tauon neutrino.

The leptons therefore, like the quarks, come in six basic "flavors" in three families—the electron and electron neutrino, the muon and muon neutrino, and the tauon and tauon neutrino. Neutrinos, originally proposed to be massless, may actually have very tiny masses and also may be able to change flavor.

These neutrino features explain some longstanding puzzles in astronomy and astrophysics, including the so-called "solar neutrino deficit." On the other hand, this observation also necessitates a modification of the Standard Model of particle interactions.

The Standard Model Describes Interactions of Fermions and Bosons

Yet another means of categorizing the fundamental particles has to do with another property, angular momentum. When dealing with elementary particles, this property is *quantized* (i.e., it can assume only certain discrete values) and characterized by a so-called spin quantum number.

For example, all quarks and leptons have odd half-integral spin and are known as *fermions*. Particles with zero or integral spin values are known as *bosons*.

Categorizing particles based on their spin actually proved to be of great significance. It turns out that

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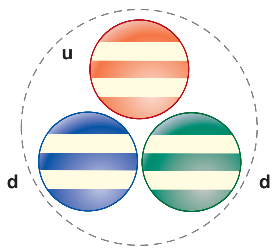
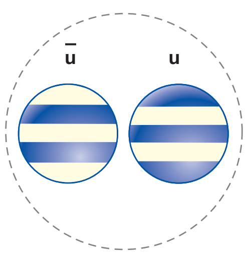
The Standard Model — *a theoretical framework that describes the strong, weak, and electromagnetic forces (but not gravity) by which the elementary building blocks (quarks and leptons) interact. It proposes that quarks and leptons make up matter, whereas bosons function as the force carriers.*

NEUTRON





NEGATIVE PI-MESON

the fundamental building blocks of matter, the quarks and leptons, are all fermions. Particles that mediate the forces of nature (gravity, electromagnetism, weak interaction, and strong force) are all bosons.

In addition to the photon (which mediates electromagnetism), other bosons mediate the other interactions: the graviton (the proposed mediator of gravity), the weak boson particles W^-, W^+, and Z^0 (which mediate the weak interaction), and gluons (mediators of the strong force). Photons, gravitons, and gluons are massless, but the W^-, W^+, and Z^0 particles do posses mass.

The behavior of bosons and fermions are fundamentally different and governed by vastly different quantum rules: bosons follow statistical laws known as Bose-Einstein statistics, whereas fermions follow Fermi-Dirac statistics.

One example of such a difference is illustrated by the behavior of electrons in an atom. As fermions, electrons must follow Fermi-Dirac statistics, including the Pauli exclusion principle. This, simply stated, asserts that no two electrons in a given atom can occupy the exact same quantum state.

Photons, being bosons, do not obey the Pauli exclusion principle and actually have a propensity to congregate in the same quantum state. This property accounts for the behavior of lasers, which produce intense, coherent beams of visible light photons.

The Pauli exclusion principle, like the conservation laws is one of the fundamentals of physics that has withstood the tests of time and experimental challenge. Therefore, when confronted by a few unusual features of certain hadrons that appeared to violate this principle, there was naturally a bit of concern.

For example, the omega minus (Ω^-) particle is composed of three *strange* quarks apparently all in the same quantum state. This would appear to violate the Pauli principle, since quarks, as fermions, should not be able to so congregate. The two ways out of the dilemma are that quarks do not obey the exclusion principle or that the three strange quarks in Ω^- are somehow different.

Just as the neutrino was proposed to explain quirks of β decay because the alternative (abandoning the laws of conservation of momentum and energy) was so abhorrent, scientists understandably were reluctant to discard the reliable Pauli exclusion principle. The proposed solution was that the quarks in Ω^- were not exactly identical, but they differed in some subtle way and therefore did not violate the exclusion principle.

This distinguishing feature was given the name *color*, and quarks were proposed to exist in three different colors: red, blue, and green.

While quarks of course do not really come in "colors," the analogy works well for another reason, one familiar to painters and photographers: The observed hadrons are always color-neutral or "white." This is because they are composed of quarks in combinations that cancel out color.

For instance, baryons are made of three quarks of different colors (red, blue, and green), which cancel out to give white. In contrast, mesons are made of quark/antiquark pairs with colors and "anticolors" (e.g., blue and "anti-blue"). The net result is that only particles of zero net color are ever observed. This would also explain why baryons are made of three quarks and mesons are made of quark/antiquark pairs—these are the only combinations that can yield net zero color.

Gluons Mediate the Strong Nuclear Force

The fundamental particles that mediate the strong nuclear force are bosons given the name *gluons*, because they serve as the "glue" holding hadrons together.

The Fundamental Forces and Their Bosons

Force/ Interaction	Boson	Boson Mass (GeV)	Relative Strength	Range (m)
Electromagnetism	Photon	0	$\sim 10^{-2}$	∞
Strong	Gluons (n = 8)	0	1	$\sim 10^{-15}$
Weak	W^+, W^-, Z^0	81–93	$\sim 10^{-13}$	$\sim 10^{-18}$
Gravity	Graviton	0	$\sim 10^{-38}$	∞

The fundamental forces are each mediated by a boson. The strong nuclear force is mediated by eight gluons, each of which carries a color and an anticolor. Emission or absorption of a gluon by a quark results in a color change in that quark. The graviton remains hypothetical.

In one very peculiar way, the strong force differs substantially from the other interactions. When distance between quarks increases, the attractive force increases rather than decreasing as the square of the distance, as it does in gravity and electromagnetism. This is explained by an increase in the number of mediating gluons when the quarks are separated farther.

This results in a phenomenon known as *particle confinement*—quarks are free to roam about within hadrons but are forever confined to hadrons.

It is suspected that free quarks might never be observed. The theory of quark confinement appears related to the rule of only "white" or colorless particles ever being observed in nature. Because quarks themselves are colored, but confined, we might expect never to observe colored particles, unless these rules can be broken.

Gluons themselves carry color (technically color and anti-color) and have the ability to change the color of the quarks they interact with. Thus, there is a gluon that converts a red quark to green, one that converts green to red, and so on. A total of eight gluons hypothetically exist to account for all the possible color changes.

The branch of physics dealing with colored quarks, gluons, and their strong interactions is called *quantum chromodynamics*. Like its forerunner, quantum electrodynamics, this is one of the most quantitatively accurate and precise theories in all of science, with numerous examples of experimental verification.

In summary, the bosons consist of 8 gluons responsible for the strong force, the photon for the electromagnetic force, the graviton for the gravitational force, and three mediators of the weak interaction, for a total of 13 force-mediating bosons.

There are six flavors of quarks in three colors for a total of 18. Including their anti-particles, this brings the total number of quarks to 36. There are six flavors of leptons, and including their anti-particles makes a total of 12.

These then are the matter-comprising and force-mediating particles of the Standard Model of particle physics. It is a far cry from the simple world of the electron, proton, and neutron but provides a logical and experimentally validated summary of the subatomic world as we now know it.

It also provides the framework for further unification of the forces. For example, we now appreciate that electricity and magnetism are really the same force with slightly different manifestations in the familiar world we live in. At higher temperatures, electromagnetism and the weak interaction are also unified as an electroweak interaction.

The successful unification of these apparently disparate interactions into one mathematically cohesive theory has led physicists to propose all-encompassing unification schemes that also enroll the

Higgs Boson—
a hypothetical particle, predicted to exist by the Standard Model, that gives mass to other particles. The Higgs boson (also known as the God particle) is responsible for the spontaneous breaking of the electroweak symmetry that exists at high temperatures, linking electromagnetic force, mediated by the massless photon, and the weak force, mediated by the massive W^-, W^+, and Z^0 particles. Interactions with the short-lived Higgs boson give mass to the W and Z particles, as well as to quarks and leptons.

strong force into Grand Unification Theories or even pull in gravity into a Theory of Everything.

Clinical Applications of Particle Physics Abound

Through this brief foray into the subatomic world, we see that there is more to radiation therapy than might be appreciated. The mundane radiation routinely prescribed for the treatment of cancer is most frequently in the form of high-energy x-ray or γ-ray photons, which we now see are the bosons that mediate the electromagnetic interaction.

As photon beam technology improved through higher energy x-ray generators, cobalt-60 γ-ray units, and finally, dedicated medical linear accelerators, the energy of the available beams increased progressively. This resulted in a considerable improvement in the radiation dosimetry of the beams such that the depth of penetration was increased and skin dose (an initially limiting factor) was significantly reduced. Acute toxicity was thereby reduced substantially, making radiation therapy more clinically applicable.

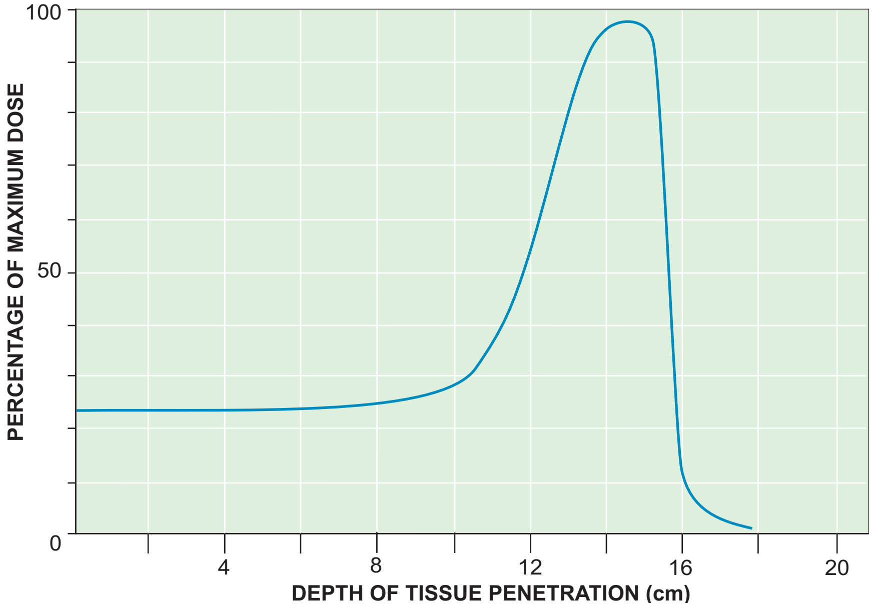
In addition to these high-energy bosons, most North American radiation oncology facilities regularly administer electron beam radiotherapy. Electrons are far less penetrating than photons and therefore have distinct advantages over photons in certain clinical situations, such as superficial malignancies and dermatologic conditions not amenable to surgical management. Electrons also are frequently used in breast-conserving management of invasive and intraductal breast cancer during the lumpectomy bed "boost" because of their reduced penetration into underlying normal lung tissue.

The electron's antiparticle, the positron, is now familiar to all oncologists through the rapidly expanding use of positron emission tomography (PET) in diagnostic, staging, and follow-up evaluations. When these antimatter particles encounter electrons, they mutually annihilate, releasing their mass-energy in the form of two 511 keV γ-photons heading 180° away from each other. When the PET detector receives simultaneous signals 180° apart, it reconstructs the source of these γ-rays, thereby identifying regions accumulating the radioactive tracer (usually ^{18}F-fluorodeoxyglucose). Because malignant tissues are frequently more metabolically active than normal tissues, they accumulate this glucose analogue more readily and are brighter on PET.

We now see that electrons and positrons belong to the lepton family of particles due to their lack of susceptibility to the strong nuclear force and are femions because of their half-integral spin. As leptons, their mass is relatively low, and therefore when positron-electron mutual annihilation occurs, the resultant γ-photons are of a modest energy that falls into the range of what is easily detected with current technology.

Their quark-composed counterparts, the hadrons, by definition interact via the strong nuclear force are also fermions, thanks to their half-integral spin. Hadron therapy is relatively rare in the United States or elsewhere, with only a handful of sites offering treatment with protons or neutrons; therapy with pi-mesons, atomic nuclei, and heavy ions has fallen out of favor due to costs, impracticality, and improvements in other technologies.

However, because of some inherent radiobiologic and dosimetric advantages, hadron therapy is making a strong comeback. One such advantage is illustrated by the way proton therapy capitalizes on the so-called Bragg peak in the depth-dose curve. Dose deposition from a monoenergetic proton beam is low on entry and remains relatively low until just before the end of the proton's range, where it rises sharply to a maximum This sharp maximum of radiation dose deposi-



The Bragg peak of an unmodified monoenergetic proton beam. The dose is moderate leading up to the peak, then rises sharply and falls abruptly to near zero. In clinical practice, the Bragg peak is spread out through the use of filters to obtain a broad, flat plateau, but the dose still falls off rapidly after the peak.

tion is known as the Bragg peak, and the dose rapidly falls to zero after this peak.

Besides protons, other charged hadron beams also exhibit a Bragg peak.

Neutron beams do not possess the dosimetric advantage of a Bragg peak but do have some radiobiologic advantages. Neutrons deposit energy very densely along their tracks and therefore are considered to have very high linear energy transfer (LET). This higher LET, in turn, is correlated with a higher relative biologic effectiveness (RBE) for tumor cell kill. (RBE is measured by the relative effectiveness of a given radiation compared to an arbitrary standard radiation of 250 keV x-rays.)

The higher effectiveness of neutrons compared to photons is due to several biologic differences, including a reduced capacity for DNA-damage repair and a reduced variation in radiosensitivity through the cell cycle with neutron irradiation.

In addition, neutrons have less dependence on oxygen to carry out their biologic effect. This is theoretically advantageous for large tumors with a high percentage of hypoxic cells. Such cells are relatively resistant to low-LET radiation, and this resistance in principle can be overcome through the use of high-LET radiation.

The initial use of neutrons in the United States and elsewhere was hampered by inadequate depth of dose deposition, leading to significant late side effects. There also were practical limitations associated with the fact that treatments were administered at physics research facilities rather than dedicated clinics or hospitals.

However, clinical trials did reveal a superiority of neutrons in certain situations, including slow-growing tumors such as salivary gland tumors, prostate cancer, and soft-tissue sarcomas. A few modern hospital-based facilities are now operational and provide treatment with improved dose-rates, dose-penetration, and practicality for patients.

Another form of hadron-based therapy is boron neutron capture therapy (BNCT), in which low-energy ("slow") neutrons are used to induce nuclear fission of boron-10 nuclei. This yields high-LET, high-RBE daughter products—helium nuclei (i.e., α-particles) and lithium nuclei. If the boron isotopes could be selectively and sufficiently concentrated within malignant tissues, this type of hadron radiotherapy has great potential for tumor destruction.

See the paper by Jacquelyn C. Yanch, Ruth E. Shefer, and Paul M. Busse on "Boron Neutron Capture Therapy" in the January/February 1999 issue of Science & Medicine (vol 6, no 1, page 18).

Therapy with beams of negatively charged pions, atomic nuclei, or "heavy" ions (e.g., carbon, neon) was proposed and used in a few locations with the hope of combining the dosimetric advantages of protons with the radiobiologic advantages of neutrons. Unfortunately, technical limitations stemming from the fact that these facilities were designed for high-energy particle physics research rather than radiation therapy, along with the costs and inaccessibility of such facilities, limited such hadron therapy to only a few sites worldwide.

Additionally, huge strides have been made recently in photon-based therapy, reducing the perceived need for complex, expensive, and impractical hadron therapy. For instance, 3-dimensional conformal radiation therapy (3D CRT) and intensity-modulated radiation therapy (IMRT) are means of manipulating photon beams that produce radiation dose deposition profiles previously unimaginable with photons. This technology thereby significantly closed the gap with hadron therapy.

However, as with any active technology-driven area of science or medicine, progress marches onward rapidly. The techniques of intensity modulation and beam shaping are now being applied to proton therapy to further augment the already superior dosimetric characteristics. Several facilities dedicated specifically for proton therapy now exist and more are currently under construction.

The disciplines of particle physics and radiation biology constitute the backbone of this fascinating and continuously evolving field of medicine. In a little over a century since its inception, radiation therapy has progressed into a extremely technologically advanced medical subspecialty now capable of achieving many of the goals initially sought. Through continued interdisciplinary collaboration, it will undoubtedly advance further, providing ever-improving outcomes for the patients in need.

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